(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
27 February 2003 (27.02.2003)

PCT

(10) International Publication Number
WO 03/015518 A1

(51) International Patent Classification[7]: A01N 43/56, C07D 401/04, 231/16, 231/14, 413/04

(21) International Application Number: PCT/US02/25613

(22) International Filing Date: 13 August 2002 (13.08.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/311,919 13 August 2001 (13.08.2001) US
60/324,173 21 September 2001 (21.09.2001) US

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(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),

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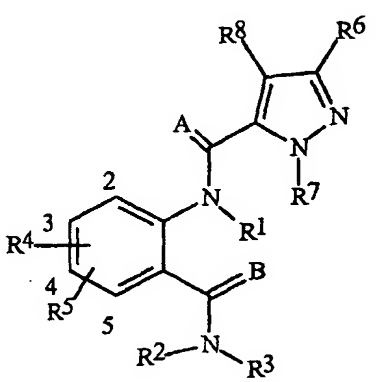
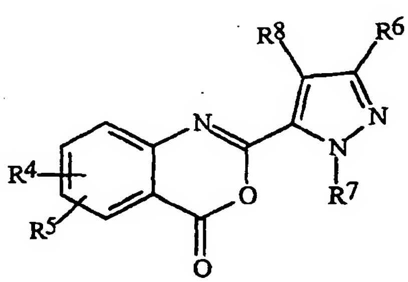
(54) Title: METHOD FOR CONTROLLING PARTICULAR INSECT PESTS BY APPLYING ANTHRANILAMIDE COMPOUNDS



(I)



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(57) Abstract: This invention pertains to a method for controlling lepidopteran, homopteran, hemipteran, thysanopteran and coleopteran insect pests comprising contacting the insects or their environment with an arthropodicidally effective amount of a compound of Formula I, its *N*-oxide or an agriculturally suitable salt thereof wherein A and B and R_1 through R_8 are as defined in the disclosure. This invention further relates to a bezoxazinone compound of Formula (10), wherein R_4 through R_8 are as defined in the disc losure, useful for preparation of a compound of Formula I.

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European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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— *of inventorship (Rule 4.17(iv)) for US only*

Published:

— *with international search report*

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TITLE

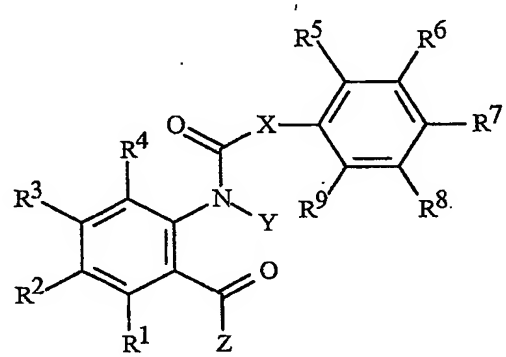
METHOD FOR CONTROLLING PARTICULAR INSECT PESTS BY APPLYING ANTHRANILAMIDE COMPOUNDS

BACKGROUND OF THE INVENTION

This invention relates to a method of use for controlling invertebrate pests in both agronomic and nonagronomic environments of certain anthranilamides, their *N*-oxides, agriculturally suitable salts and compositions.

The control of invertebrate pests is extremely important in achieving high crop efficiency. Damage by invertebrate pests to growing and stored agronomic crops can cause significant reduction in productivity and thereby result in increased costs to the consumer. The control of invertebrate pests in forestry, greenhouse crops, ornamentals, nursery crops, stored food and fiber products, livestock, household, and public and animal health is also important. Many products are commercially available for these purposes, but the need continues for new compounds that are more effective, less costly, less toxic, environmentally safer or have different modes of action.

NL 9202078 discloses *N*-acyl anthranilic acid derivatives of Formula i as insecticides



i

wherein, *inter alia*,

X is a direct bond;

Y is H or C_1–C_6 alkyl;

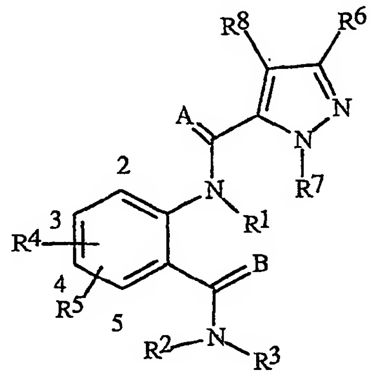
Z is NH_2, $NH(C_1–C_3$ alkyl) or $N(C_1–C_3$ alkyl$)_2$; and

R^1 through R^9 are independently H, halogen, C_1–C_6 alkyl, phenyl, hydroxy, C_1–C_6 alkoxy or C_1–C_7 acyloxy.

SUMMARY OF THE INVENTION

This invention pertains to a method for controlling lepidopteran, homopteran, hemipteran, thysanopteran and coleopteran insect pests comprising contacting the insects or

their environment with an arthropodicidally effective amount of a compound of Formula **I**, its *N*-oxide or an agriculturally suitable salt thereof



I

wherein

A and B are independently O or S;

R^1 is H, C_1-C_6 alkyl, C_2-C_6 alkoxycarbonyl or C_2-C_6 alkylcarbonyl;

R^2 is H or C_1-C_6 alkyl;

R^3 is H; C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, or C_3-C_6 cycloalkyl, each optionally substituted with one or more substituents selected from the group consisting of halogen, CN, NO_2, hydroxy, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_2-C_6 alkoxycarbonyl, C_2-C_6 alkylcarbonyl, C_3-C_6 trialkylsilyl, phenyl, phenoxy, 5-membered heteroaromatic rings, and 6-membered heteroaromatic rings; each phenyl, phenoxy, 5-membered heteroaromatic ring, and 6-membered heteroaromatic ring optionally substituted with one to three substituents independently selected from the group consisting of C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_3-C_6 cycloalkyl, C_1-C_4 haloalkyl, C_2-C_4 haloalkenyl, C_2-C_4 haloalkynyl, C_3-C_6 halocycloalkyl, halogen, CN, NO_2, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_4 alkylamino, C_2-C_8 dialkylamino, C_3-C_6 cycloalkylamino, C_4-C_8 (alkyl)(cycloalkyl)amino, C_2-C_4 alkylcarbonyl, C_2-C_6 alkoxycarbonyl, C_2-C_6 alkylaminocarbonyl, C_3-C_8 dialkylaminocarbonyl and C_3-C_6 trialkylsilyl; C_1-C_4 alkoxy; C_1-C_4 alkylamino; C_2-C_8 dialkylamino; C_3-C_6 cycloalkylamino; C_2-C_6 alkoxycarbonyl or C_2-C_6 alkylcarbonyl;

R^4 is H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_1-C_6 haloalkyl, CN, halogen, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy or NO_2;

R^5 is H, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_4 alkoxyalkyl, C_1-C_4 hydroxyalkyl, $C(O)R^{10}$, CO_2R^{10}, $C(O)NR^{10}R^{11}$, halogen, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, $NR^{10}R^{11}$, $N(R^{11})C(O)R^{10}$, $N(R^{11})CO_2R^{10}$ or $S(O)_nR^{12}$;

R^6 is H, C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, CN, C_1-C_4 alkoxy or C_1-C_4 haloalkoxy;

R^7 is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_1-C_6 haloalkyl, C_2-C_6 haloalkenyl, C_2-C_6 haloalkynyl or C_3-C_6 halocycloalkyl; or

R^7 is a phenyl ring, a benzyl ring, a 5- or 6-membered heteroaromatic ring, a naphthyl ring system or an aromatic 8-, 9- or 10-membered fused heterobicyclic ring system, each ring or ring system optionally substituted with one to three substituents independently selected from R^9;

R^8 is H, C_1–C_6 alkyl, C_1–C_6 haloalkyl, halogen, C_1–C_4 alkoxy or C_1–C_4 haloalkoxy;

each R^9 is independently C_1–C_4 alkyl, C_2–C_4 alkenyl, C_2–C_4 alkynyl, C_3–C_6 cycloalkyl, C_1–C_4 haloalkyl, C_2–C_4 haloalkenyl, C_2–C_4 haloalkynyl, C_3–C_6 halocycloalkyl, halogen, CN, NO_2, C_1–C_4 alkoxy, C_1–C_4 haloalkoxy, C_1–C_4 alkylthio, C_1–C_4 alkylsulfinyl, C_1–C_4 alkylsulfonyl, C_1–C_4 alkylamino, C_2–C_8 dialkylamino, C_3–C_6 cycloalkylamino, C_4–C_8 (alkyl)(cycloalkyl)amino, C_2–C_4 alkylcarbonyl, C_2–C_6 alkoxycarbonyl, C_2–C_6 alkylaminocarbonyl, C_3–C_8 dialkylaminocarbonyl or C_3–C_6 trialkylsilyl;

R^{10} is H, C_1–C_4 alkyl or C_1–C_4 haloalkyl;

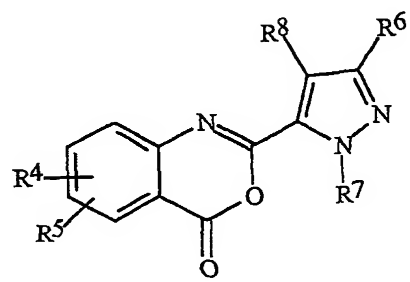
R^{11} is H or C_1–C_4 alkyl;

R^{12} is C_1–C_4 alkyl or C_1–C_4 haloalkyl; and

n is 0, 1 or 2.

This invention also relates to such a method wherein an invertebrate pest or its environment is contacted with a composition comprising a biologically effective amount of a compound of Formula **I** or a composition comprising a compound of Formula **I** and a biologically effective amount of at least one additional biologically active compound.

This invention further relates to a benzoxazinone compound of Formula **10**



10

wherein

R^4, R^5, R^6, R^7 and R^8 are defined as aboved in Formula I.

The compound of Formula **10** is useful as a synthetic intermediate for preparing a compound of Formula I.

DETAILS OF THE INVENTION

In the above recitations, the term "alkyl", used either alone or in compound words such as "alkylthio" or "haloalkyl" includes straight-chain or branched alkyl, such as, methyl, ethyl, *n*-propyl, *i*-propyl, or the different butyl, pentyl or hexyl isomers. "Alkenyl" includes straight-chain or branched alkenes such as 1-propenyl, 2-propenyl, and the different butenyl, pentenyl and hexenyl isomers. "Alkenyl" also includes polyenes such as 1,2-propadienyl and 2,4-hexadienyl. "Alkynyl" includes straight-chain or branched alkynes such as 1-propynyl, 2-propynyl and the different butynyl, pentynyl and hexynyl isomers. "Alkynyl" can also include moieties comprised of multiple triple bonds such as 2,5-hexadiynyl. "Alkoxy" includes, for example, methoxy, ethoxy, *n*-propyloxy, isopropyloxy and the different butoxy, pentoxy and hexyloxy isomers. "Alkoxyalkyl" denotes alkoxy substitution on alkyl. Examples of "alkoxyalkyl" include CH_3OCH_2, $CH_3OCH_2CH_2$, $CH_3CH_2OCH_2$, $CH_3CH_2CH_2CH_2OCH_2$ and $CH_3CH_2OCH_2CH_2$. "Alkylthio" includes branched or straight-chain alkylthio moieties such as methylthio, ethylthio, and the different propylthio, butylthio, pentylthio and hexylthio isomers. "Cycloalkyl" includes, for example, cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl.

The term "heterocyclic ring" or heterocyclic ring system" denotes rings or ring systems in which at least one ring atom is not carbon and comprises 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, oxygen and sulfur, provided that each heterocyclic ring contains no more than 4 nitrogens, no more than 2 oxygens and no more than 2 sulfurs. The heterocyclic ring can be attached through any available carbon or nitrogen by replacement of hydrogen on said carbon or nitrogen. The term "aromatic ring system" denotes fully unsaturated carbocycles and heterocycles in which at least one ring of the polycyclic ring system is aromatic (where aromatic indicates that the Hückel rule is satisfied for the ring system). The term "heteroaromatic ring" denotes fully aromatic rings in which at least one ring atom is not carbon and comprises 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, oxygen and sulfur, provided that each heterocyclic ring contains no more than 4 nitrogens, no more than 2 oxygens and no more than 2 sulfurs (where aromatic indicates that the Hückel rule is satisfied). The heterocyclic ring can be attached through any available carbon or nitrogen by replacement of hydrogen on said carbon or nitrogen. The term "aromatic heterocyclic ring system" includes fully aromatic heterocycles and heterocycles in which at least one ring of a polycyclic ring system is aromatic (where aromatic indicates that the Hückel rule is satisfied). The term "fused heterobicyclic ring system" includes a ring system comprised of two fused rings in which at least one ring atom is not carbon and can be aromatic or non aromatic, as defined above.

The term "halogen", either alone or in compound words such as "haloalkyl", includes fluorine, chlorine, bromine or iodine. Further, when used in compound words such as "haloalkyl", said alkyl may be partially or fully substituted with halogen atoms which may be the same or different. Examples of "haloalkyl" include F_3C, $ClCH_2$, CF_3CH_2 and CF_3CCl_2. The terms "haloalkenyl", "haloalkynyl", "haloalkoxy", and the like, are defined analogously to the term "haloalkyl". Examples of "haloalkenyl" include $(Cl)_2C{=}CHCH_2$ and $CF_3CH_2CH{=}CHCH_2$. Examples of "haloalkynyl" include $HC{\equiv}CCHCl$, $CF_3C{\equiv}C$, $CCl_3C{\equiv}C$ and $FCH_2C{\equiv}CCH_2$. Examples of "haloalkoxy" include CF_3O, CCl_3CH_2O, $HCF_2CH_2CH_2O$ and CF_3CH_2O.

The total number of carbon atoms in a substituent group is indicated by the "C_i–C_j" prefix where i and j are numbers from 1 to 8. For example, C_1–C_4 alkylsulfonyl designates methylsulfonyl through butylsulfonyl; C_2 alkoxyalkyl designates CH_3OCH_2; C_3 alkoxyalkyl designates, for example, $CH_3CH(OCH_3)$, $CH_3OCH_2CH_2$ or $CH_3CH_2OCH_2$; and C_4 alkoxyalkyl designates the various isomers of an alkyl group substituted with an alkoxy group containing a total of four carbon atoms, examples including $CH_3CH_2CH_2OCH_2$ and $CH_3CH_2OCH_2CH_2$. In the above recitations, when a compound of Formula **I** comprises a heterocyclic ring, all substituents are attached to this ring through any available carbon or nitrogen by replacement of a hydrogen on said carbon or nitrogen.

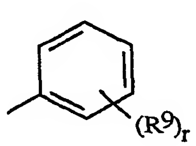
The term "optionally substituted with one to three substituents" indicates that one to three of the available positions on the group may be substituted. When a group contains a substituent which can be hydrogen, for example R^6, then, when this substituent is taken as hydrogen, it is recognized that this is equivalent to said group being unsubstituted.

Compounds of Formula **I** can exist as one or more stereoisomers. The various stereoisomers include enantiomers, diastereomers, atropisomers and geometric isomers. One skilled in the art will appreciate that one stereoisomer may be more active and/or may exhibit beneficial effects when enriched relative to the other stereoisomer(s) or when separated from the other stereoisomer(s). Additionally, the skilled artisan knows how to separate, enrich, and/or to selectively prepare said stereoisomers. Accordingly, the compounds of Formula **I** may be present as a mixture of stereoisomers, individual stereoisomers, or as an optically active form. Similarly, compounds of Formula **10** can exist as one or more stereoisomers. The various stereoisomers include enantiomers, diastereomers, atropisomers and geometric isomers. One skilled in the art will appreciate that one stereoisomer of a compound of Formula **10** may be more useful in preparing a specific stereoisomer of Formula **I**. Additionally, the skilled artisan knows how to separate, enrich, and/or to selectively prepare said stereoisomers. Accordingly, the compounds of Formula **10** may be present as a mixture of stereoisomers, individual stereoisomers, or as an optically active form.

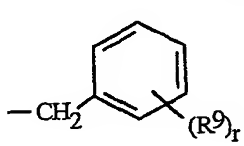
The salts of the compounds of Formula **I** include acid-addition salts with inorganic or organic acids such as hydrobromic, hydrochloric, nitric, phosphoric, sulfuric, acetic, butyric, fumaric, lactic, maleic, malonic, oxalic, propionic, salicylic, tartaric, 4-toluenesulfonic or valeric acids.

As noted above, R^7 is (among others) a phenyl, a benzyl, a 5- or 6-membered heteroaromatic ring, a naphthyl ring system or an aromatic 8-, 9- or 10-membered fused heterobicyclic ring system, each ring or ring system optionally substituted with one to three substituents independently selected from R^9. The term "optionally substituted" in connection with these R^7 groups refers to groups which are unsubstituted or have at least one non-hydrogen substituent that does not extinguish the invertebrate pest control activity possessed by the unsubstituted analog. Note also that J-1 through J-4 below denote 5- or 6-membered heteroaromatic rings. An example of a phenyl ring optionally substituted with 1 to 3 R^9 is the ring illustrated as J-5 in Exhibit 1, wherein r is an integer from 0 to 3. An example of a benzyl ring optionally substituted with 1 to 3 R^9 is the ring illustrated as J-6 in Exhibit 1, wherein r is an integer from 0 to 3. An example of a naphthyl ring system optionally substituted with 1 to 3 R^9 is illustrated as J-59 in Exhibit 1, wherein r is an integer from 0 to 3. Examples of a 5- or 6-membered heteroaromatic ring optionally substituted with 1 to 3 R^9 include the rings J-7 through J-58 illustrated in Exhibit 1 wherein r is an integer from 0 to 3. Note that J-7 through J-26 are examples of J-1, J-27 through J-41 are examples of J-2, and J-46 through J-58 are examples of J-3 and J-4. The nitrogen atoms that require substitution to fill their valence are substituted with H or R^9. Note that some J groups can only be substituted with less than 3 R^9 groups (e.g. J-19, J-20, J-23 through J-26 and J-37 through J-40 can only be substituted with one R^9). Examples of aromatic 8-, 9- or 10-membered fused heterobicyclic ring systems optionally substituted with 1 to 3 R^9 include J-60 through J-90 illustrated in Exhibit 1 wherein r is an integer from 0 to 3. Although R^9 groups are shown in the structures J-5 through J-90, it is noted that they do not need to be present since they are optional substituents. Note that when the attachment point between $(R^9)_r$ and the J group is illustrated as floating, $(R^9)_r$ can be attached to any available carbon atom of the J group. Note that when the attachment point on the J group is illustrated as floating, the J group can be attached to the remainder of Formula **I** through any available carbon of the J group by replacement of a hydrogen atom.

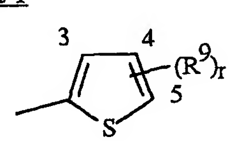
<u>Exhibit 1</u>



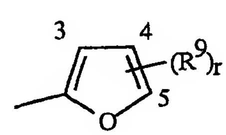
J-5,



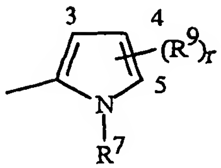
J-6,

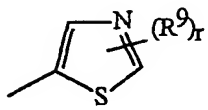


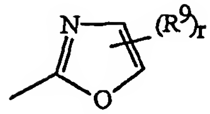
J-7,



J-8,


J-9


J-10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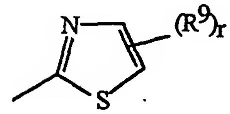
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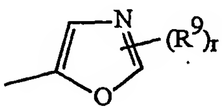
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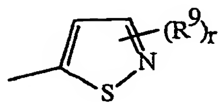
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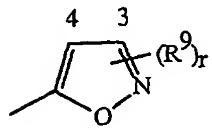
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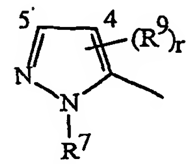
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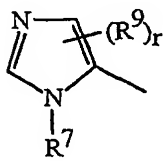
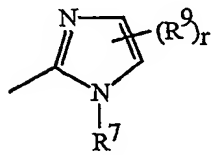

J-17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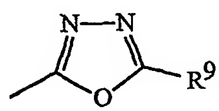
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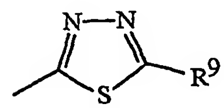
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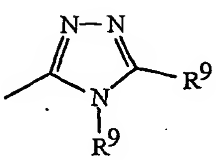
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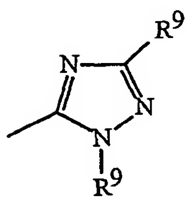
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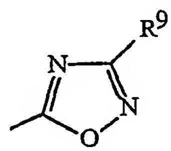
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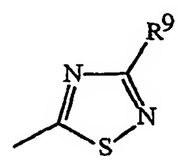
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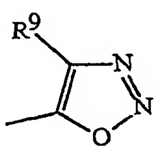
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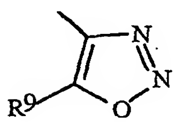
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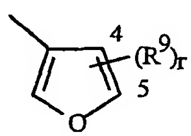
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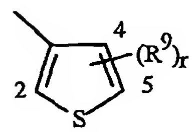
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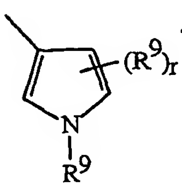
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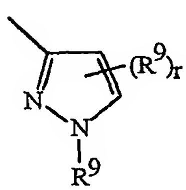
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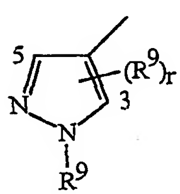
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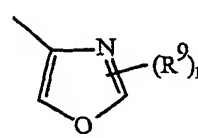
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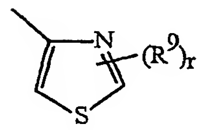
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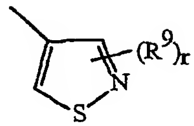
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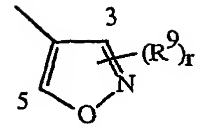
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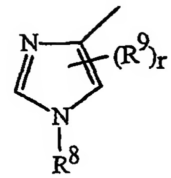
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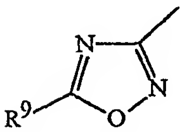
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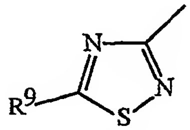
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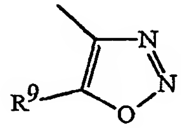
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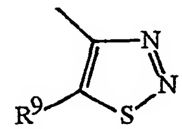
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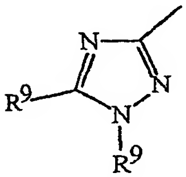
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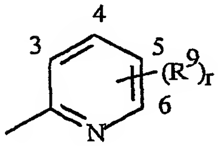
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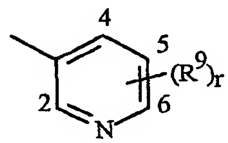
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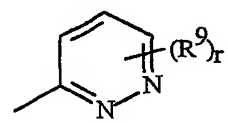
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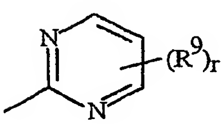
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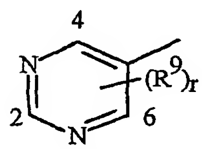
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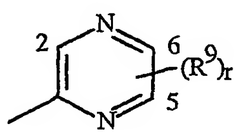
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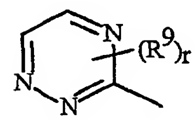
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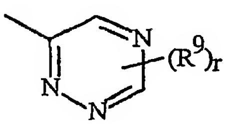
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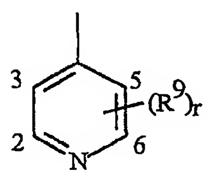
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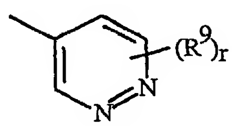
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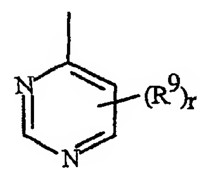
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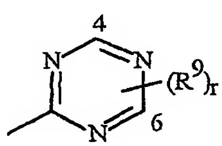
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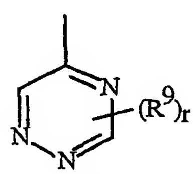
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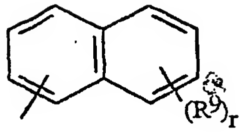
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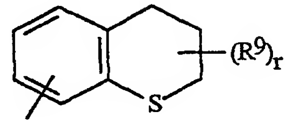
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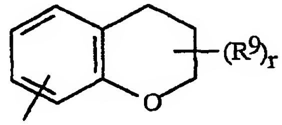
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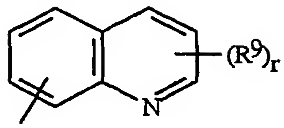 ,

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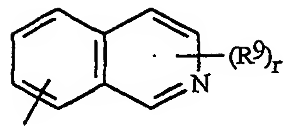 ,

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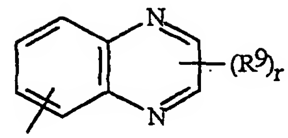 ,

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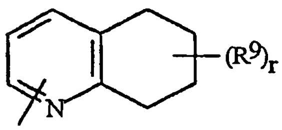 ,

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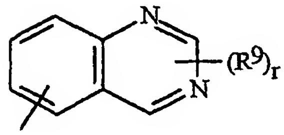 ,

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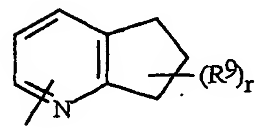 ,

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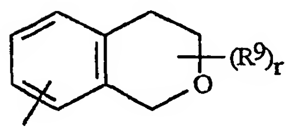 ,

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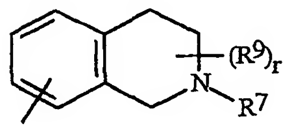 ,

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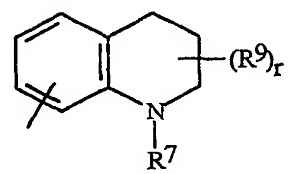 ,

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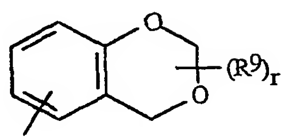 ,

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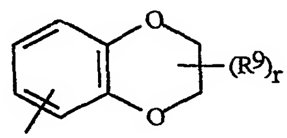 ,

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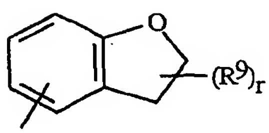 ,

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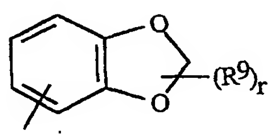 ,

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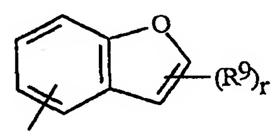 ,

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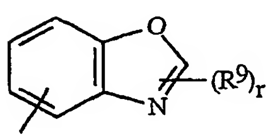 ,

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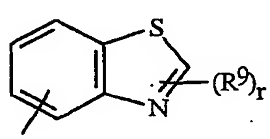 ,

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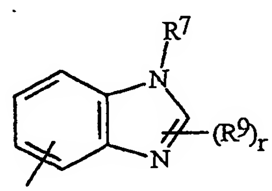 ,

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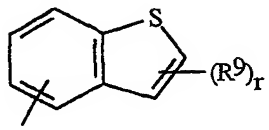,

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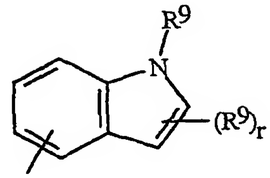,

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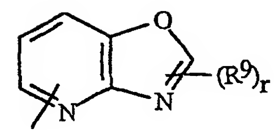,

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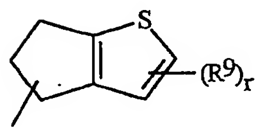,

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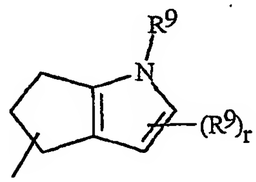,

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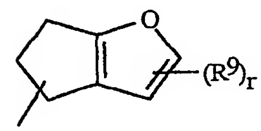,

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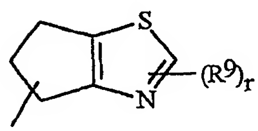,

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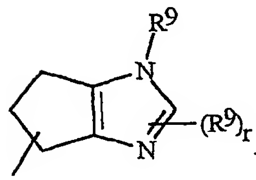,

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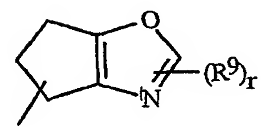,

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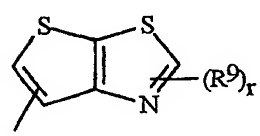,

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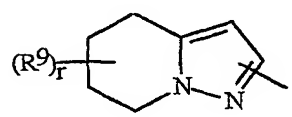

J-89

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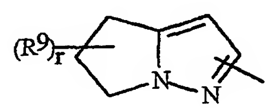

J-90

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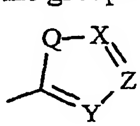
Preferred methods for reasons of cost, ease of synthesis or application, and/or biological efficacy are:

Preferred 1. Methods comprising a compound of Formula **I** wherein

A and B are both O;

R^7 is a phenyl ring or a 5- or 6-membered heteroaromatic ring selected from the group consisting of

,

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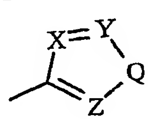,

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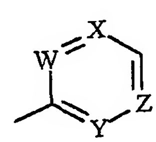
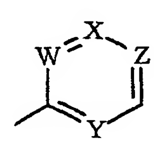


J-3

and

,

J-4

each ring optionally substituted with one to three substituents independently selected from R^9;

Q is O, S, NH or NR^9; and

W, X, Y and Z are independently N, CH or CR^9, provided that in J-3 and J-4 at least one of W, X, Y or Z is N.

Preferred 2. Methods of Preferred 1 wherein

R^1, R^2 and R^8 are all H;

R^3 is C_1-C_4 alkyl optionally substituted with halogen, CN, OCH_3 or $S(O)_pCH_3$;

R^4 group is attached at position 2;

R^4 is CH_3, CF_3, OCF_3, $OCHF_2$, CN or halogen;

R^5 is H, CH_3 or halogen;

R^6 is CH_3, CF_3 or halogen;

R^7 is phenyl or 2-pyridinyl, each optionally substituted; and

p is 0, 1 or 2.

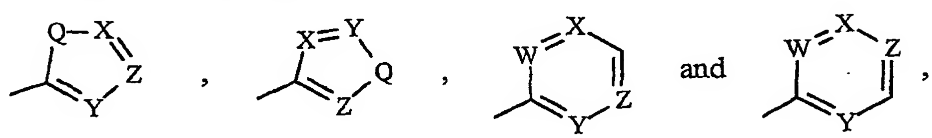
Preferred 3. Methods of Preferred 2 wherein R^3 is C_1-C_4 alkyl and R^6 is CF_3.

Preferred 4. A compound of Preferred 2 wherein R^3 is C_1-C_4 alkyl and R^6 is Cl or Br.

Preferred compounds of Formula **10** are:

Preferred A. Compounds of Formula **10** wherein

R^7 is a phenyl ring or a 5- or 6-membered heteroaromatic ring selected from the group consisting of



J-1 J-2 J-3 J-4

each ring optionally substituted with one to three substituents independently selected from R^9;

Q is O, S, NH or NR^9; and

W, X, Y and Z are independently N, CH or CR^9, provided that in J-3 and J-4 at least one of W, X, Y or Z is N.

Preferred B. Compounds of Preferred A wherein

R^8 is H;

R^4 group is attached at position 2;

R^4 is CH_3, CF_3, OCF_3, $OCHF_2$, CN or halogen;

R^5 is H, CH_3 or halogen;

R^6 is CH_3, CF_3 or halogen; and

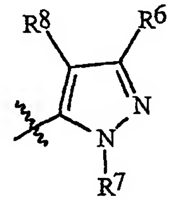
R^7 is phenyl or 2-pyridinyl, each optionally substituted.

Preferred C. Compounds of Preferred B wherein R^6 is CF_3.

Preferred D. Compounds of Preferred B wherein R^6 is Cl or Br.

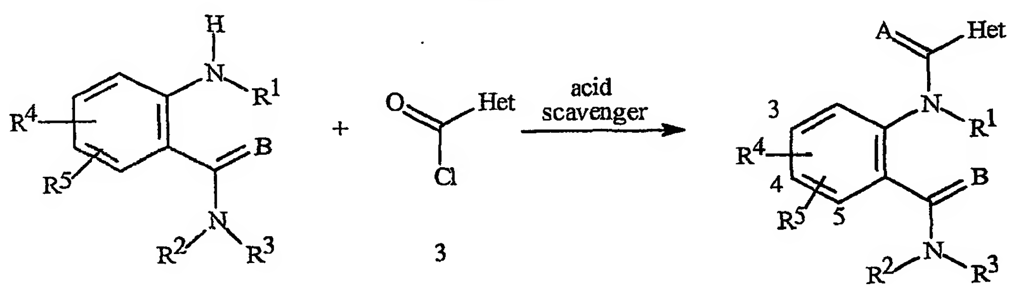
Of note are compounds of Formula **10** wherein R^4 is at the 2 position and is CH_3, Cl or Br; R^5 is at the 4 position and is F, Cl, Br, I or CF_3; R^6 is CF_3, Cl or Br; R^7 is 3-Cl-2-pyridinyl or 3-Br-2-pyridinyl; and R^8 is H.

One or more of the following methods and variations as described in Schemes 1-22 can be used to prepare the compounds of Formula **I**. The definitions of A, B and R^1 through R^9 in the compounds of Formulae **2-40** below are as defined above in the Summary of the Invention unless indicated otherwise. Compounds of Formulae **Ia-d**, **2a-d**, **3a**, **4a-d**, **5a-b**, **17a-c**, **18a** and **32a-b** are various subsets of the compounds of Formula **I**, **2**, **3**, **4**, **5**, **17**, **18** and **32**. In the schemes, Het is the moiety shown below:

Het is 

A typical method for preparation of a compound of Formula **Ia** is described in Scheme 1.

Scheme 1



2 3

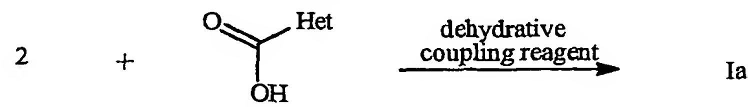
Ia (A is O)
Ib (A is S)

The method of Scheme 1 involves coupling of an amine of Formula **2** with an acid chloride of Formula **3** in the presence of an acid scavenger to provide the compound of Formula **Ia**. Typical acid scavengers include amine bases such as triethylamine, *N,N*-diisopropylethylamine and pyridine; other scavengers include hydroxides such as sodium and potassium hydroxide and carbonates such as sodium carbonate and potassium carbonate. In certain instances it is useful to use polymer-supported acid scavengers such as polymer-bound *N,N*-diisopropylethylamine and polymer-bound 4-(dimethylamino)pyridine. The coupling can be run in a suitable inert solvent such as tetrahydrofuran, dioxane, diethylether or dichloromethane to afford the anilide of Formula **Ia**.

A thioamide of Formula **Ib** can be obtained in a subsequent step from the corresponding amide of Formula **Ia** by treatment with one of a variety of standard thio transfer reagents including phosphorus pentasulfide and Lawesson's reagent (2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide).

As shown in Scheme 2, an alternate procedure for the preparation of compounds of Formula **Ia** involves coupling of an amine of Formula **2** with an acid of Formula **4** in the presence of a dehydrating agent such as dicyclohexylcarbodiimide (DCC), 1,1'-carbonyl-diimidazole, bis(2-oxo-3-oxazolidinyl)phosphinic chloride or benzotriazol-1-yloxy-tris-(dimethylamino)phosphonium hexafluorophosphate.

Scheme 2



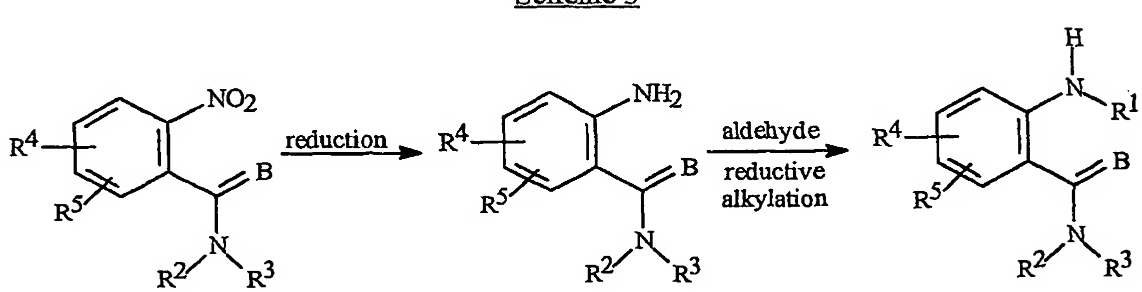
4

Polymer-supported reagents are again useful here, such as polymer-bound cyclohexylcarbodiimide. The coupling can be run in a suitable inert solvent such as dichloromethane or *N,N*-dimethylformamide. The synthetic methods of Schemes 1 and 2 are just representative examples of a wide variety of coupling methods useful for the preparation of Formula **I** compounds; the synthetic literature is extensive for this type of coupling reaction.

One skilled in the art will also realize that acid chlorides of Formula **3** may be prepared from acids of Formula **4** by numerous well-known methods. For example, acid chlorides of Formula **3** are readily made from carboxylic acids of Formula **4** by reacting the carboxylic acid **4** with thionyl chloride or oxalyl chloride in an inert solvent such as toluene or dichloromethane in the presence of a catalytic amount of *N,N*-dimethylformamide.

As shown in Scheme 3, amines of Formula **2a** are typically available from the corresponding 2-nitrobenzamides of Formula **5** via catalytic hydrogenation of the nitro group.

Scheme 3

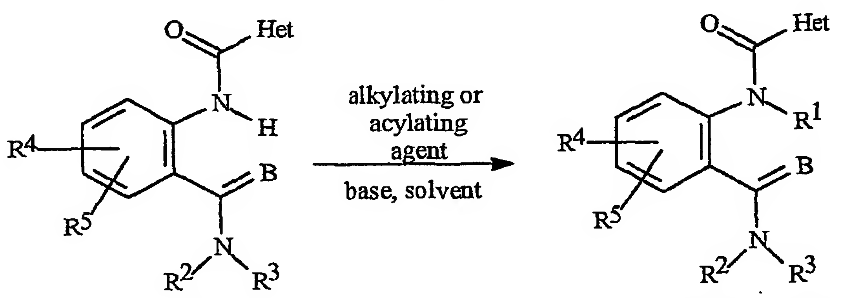


5 2a 2b (R^1 is other than H)

Typical procedures involve reduction with hydrogen in the presence of a metal catalyst such as palladium on carbon or platinum oxide and in hydroxylic solvents such as ethanol and isopropanol. Amines of Formula **2a** can also be prepared by reduction with zinc in acetic acid. These procedures are well documented in the chemical literature. R^1 substituents such as C_1-C_6 alkyl can be introduced at this stage through well known methodologies including either direct alkylation or through the generally preferred method of reductive alkylation of the amine. As is further shown in Scheme 3, a commonly employed procedure is to combine the amine **2a** with an aldehyde in the presence of a reducing agent such as sodium cyanoborohydride to produce the Formula **2b** compounds where R^1 is C_1-C_6 alkyl.

Scheme 4 shows that compounds of Formula **Ic** can be alkylated or acylated with a suitable alkylating or acylating agent such as an alkyl halide, alkyl chloroformate or acyl chloride in the presence of a base such as sodium hydride or *n*-butyllithium in an inert solvent such as tetrahydrofuran or *N,N*-dimethylformamide to afford anilides of Formula **Id** wherein R^1 is other than hydrogen.

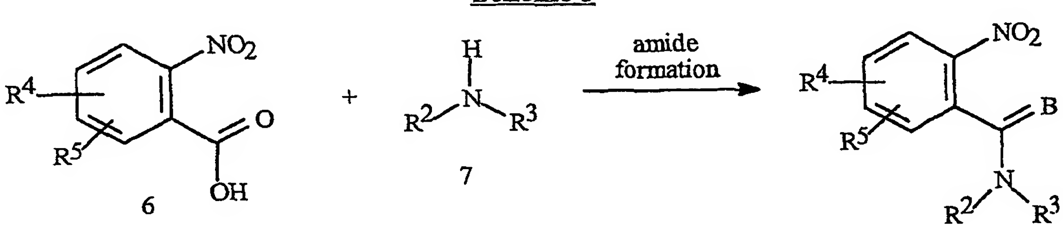
Scheme 4



Ic   Id (R^1 is other than H)

The intermediate amides of Formula **5a** are readily prepared from commercially available 2-nitrobenzoic acids. Typical methods for amide formation can be used. As shown in Scheme 5, these methods include direct dehydrative coupling of acids of Formula **6** with amines of Formula **7** using for example DCC, and conversion of the acids to activated forms such as the acid chlorides or anhydrides and subsequent coupling with amines to form amides of Formula **5a**.

Scheme 5

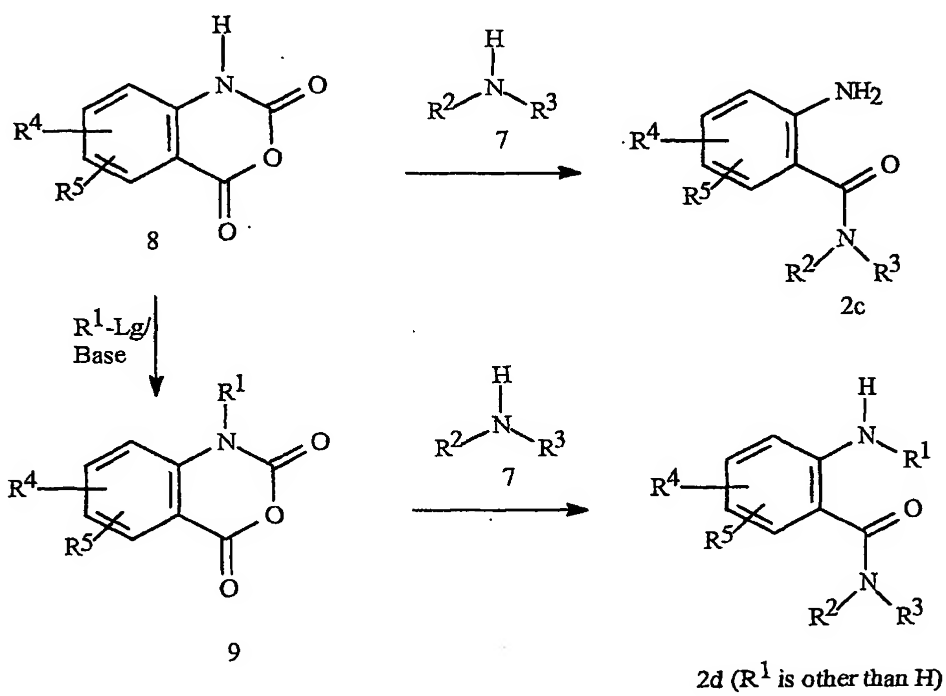


6   7   5a (B is O)
5b (B is S)

Alkyl chloroformates, such as ethyl chloroformate or isopropyl chloroformate, are especially useful reagents for this type of reaction involving activation of the acid. The chemical literature is extensive regarding methods for amide formation. Amides of Formula **5a** are readily converted to thioamides of Formula **5b** by using commercially available thio transfer reagents such as phosphorus pentasulfide and Lawesson's reagent.

Intermediate anthranilic amides of Formula **2c** or **2d** may also be prepared from isatoic anhydrides of Formula **8** or **9**, respectively, as shown in Scheme 6.

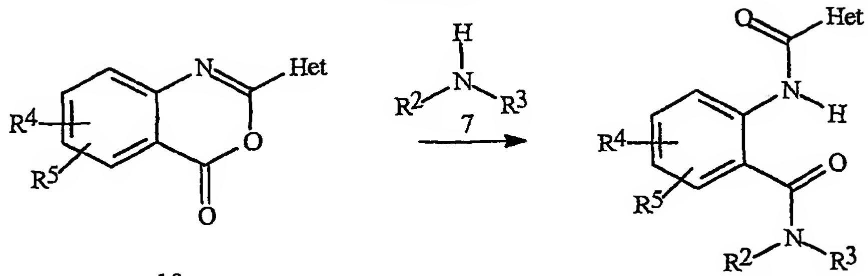
Scheme 6



Typical procedures involve combination of equimolar amounts of the amine **7** with the isatoic anhydride in polar aprotic solvents such as pyridine and *N,N*-dimethylformamide at temperatures ranging from room temperature to 100 °C. R^1 substituents such as alkyl and substituted alkyl may be introduced by the base-catalyzed alkylation of isatoic anhydride **8** with known alkylating reagents R^1-Lg (wherein Lg is a nucleophilic displaceable leaving group such as halide, alkyl or aryl sulfonates or alkyl sulfates) to provide the alkyl substituted intermediate **9**. Isatoic anhydrides of Formula **8** may be made by methods described in Coppola, *Synthesis* **1980,** 505-36.

As shown in Scheme 7, an alternate procedure for the preparation of specific compounds of Formula **Ic** involves reaction of an amine **7** with a benzoxazinone of Formula **10**.

Scheme 7

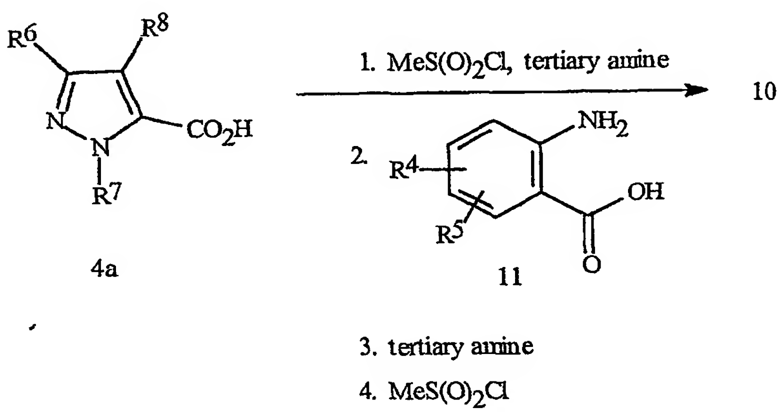


10 Ic

The reaction of Scheme 7 can be run neat or in a variety of suitable solvents including tetrahydrofuran, diethyl ether, pyridine, dichloromethane or chloroform with optimum temperatures ranging from room temperature to the reflux temperature of the solvent. The general reaction of benzoxazinones with amines to produce anthranilamides is well documented in the chemical literature. For a review of benzoxazinone chemistry see Jakobsen et al., *Biorganic and Medicinal Chemistry* **2000**, *8*, 2095-2103 and references cited therein. See also Coppola, *J. Heterocyclic Chemistry* **1999**, *36*, 563-588.

Benzoxazinones of Formula **10** can be prepared by a variety of procedures. Two procedures that are especially useful are detailed in Schemes 8-9. In Scheme 8, a benzoxazinone of Formula **10** is prepared directly via coupling of a pyrazolecarboxylic acid of Formula **4a** with an anthranilic acid of Formula **11**.

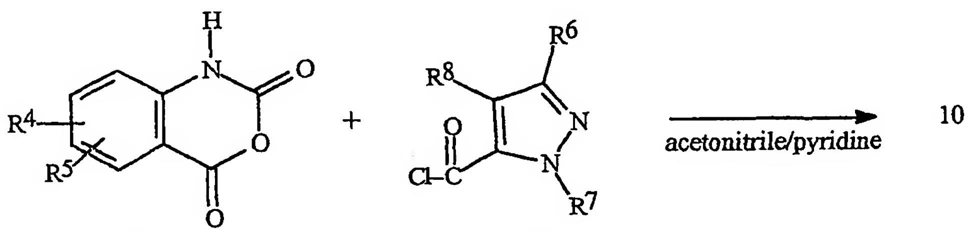
Scheme 8



This involves sequential addition of methanesulfonyl chloride in the presence of a tertiary amine such as triethylamine or pyridine to a pyrazolecarboxylic acid of Formula **4a**, followed by the addition of an anthranilic acid of Formula **11**, followed by a second addition of tertiary amine and methanesulfonyl chloride. This procedure generally affords good yields of the benzoxazinone and is illustrated with greater detail in Examples 6 and 8.

Scheme 9 depicts an alternate preparation for benzoxazinones of Formula **10** involving coupling of a pyrazole acid chloride of Formula **3a** with an isatoic anhydride of Formula **8** to provide the Formula **10** benzoxazinone directly.

Scheme 9

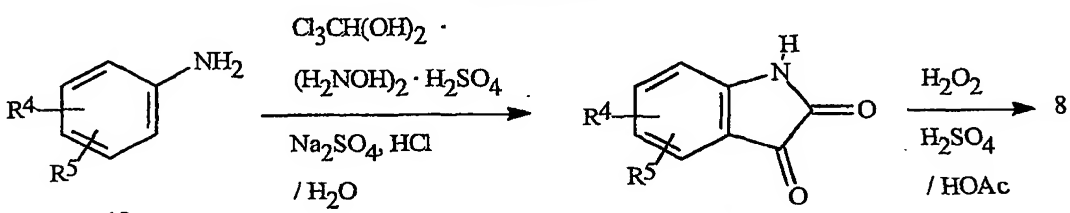


8 3a

Solvents such as pyridine or pyridine/acetonitrile are suitable for this reaction. The acid chlorides of Formula **3a** are available from the corresponding acids of Formula **4a** by a variety of synthetic methods such as chlorination with thionyl chloride or oxalyl chloride.

Isatoic anhydrides of Formula **8** can be prepared from isatins of Formula **13** as outlined in Scheme 10.

Scheme 10

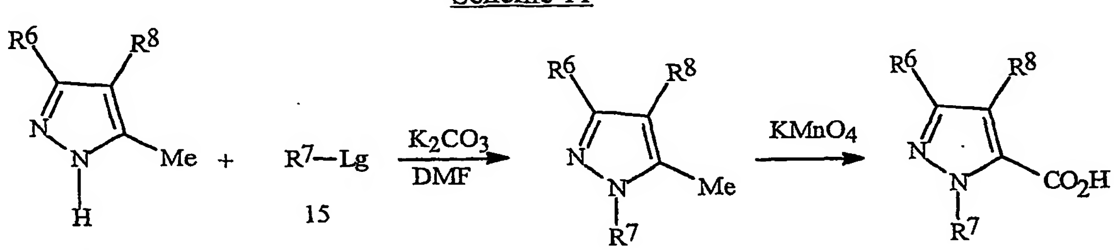


12 13

Isatins of Formula **13** are obtained from aniline derivatives of Formula **12** using methods known in the literature. Oxidation of isatin **13** with hydrogen peroxide generally affords good yields of the corresponding isatoic anhydride **8** (*Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 222-223). Isatoic anhydrides are also available from the anthranilic acids **11** via many known procedures involving reaction of **11** with phosgene or a phosgene equivalent.

The syntheses of representative acids of Formula **4** are depicted in Schemes 11-16. Syntheses of pyrazoles of Formula **4a** are shown in Scheme 11.

Scheme 11

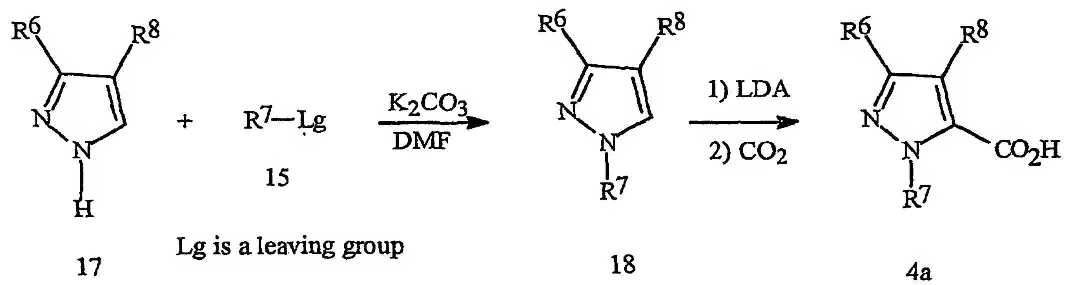


14 Lg is a leaving group 16 4a

The synthesis of compounds of Formula **4a** in Scheme 11 involves as the key step introduction of the R^7 substituent via alkylation or arylation of the pyrazole of Formula **14** with compounds of Formula **15** (wherein Lg is a leaving group as defined above). Oxidation of the methyl group affords the pyrazole carboxylic acid. Some of the more preferred R^6 groups include haloalkyl.

Synthesis of pyrazoles of Formula **4a** is also shown in Scheme 12.

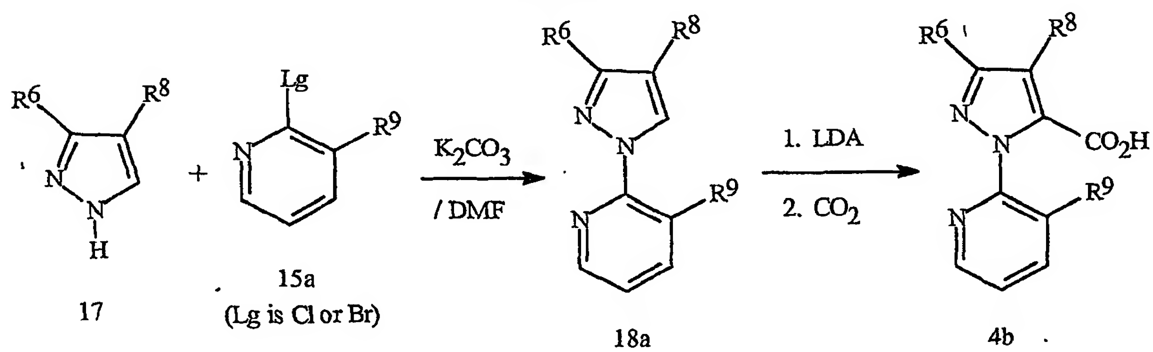
Scheme 12



These acids may be prepared via metallation and carboxylation of compounds of Formula **18** as the key step. The R^7 group is introduced in a manner similar to that of Scheme 11, i.e. via alkylation or arylation with a compound of Formula **15**. Representative R^6 groups include e.g. cyano, haloalkyl and halogen.

This procedure is particularly useful for preparing 1-(2-pyridinyl)pyrazolecarboxylic acids of Formula **4b** as shown in Scheme 13.

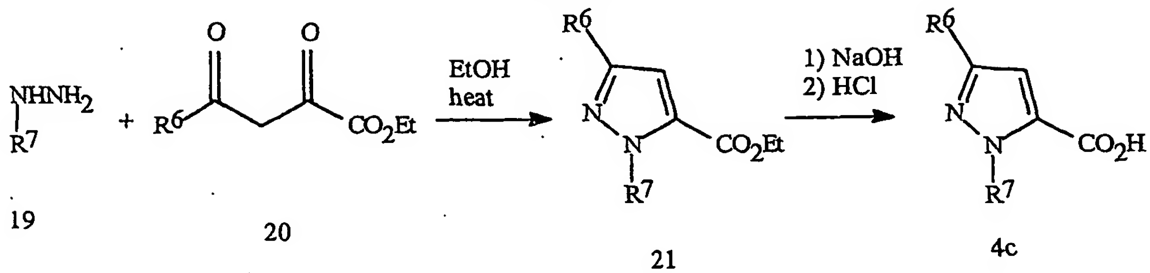
Scheme 13



Reaction of a pyrazole of Formula **17** with a 2,3-dihalopyridine of Formula **15a** affords good yields of the 1-pyridylpyrazole of Formula **18a** with good specificity for the desired regiochemistry. Metallation of **18a** with lithium diisopropylamide (LDA) followed by quenching of the lithium salt with carbon dioxide affords the 1-(2-pyridinyl)pyrazole-carboxylic acid of Formula **4b**. Additional details for these procedures are provided in Examples 1, 3, 6, 8 and 10.

The synthesis of pyrazoles of Formula **4c** is described in Scheme 14.

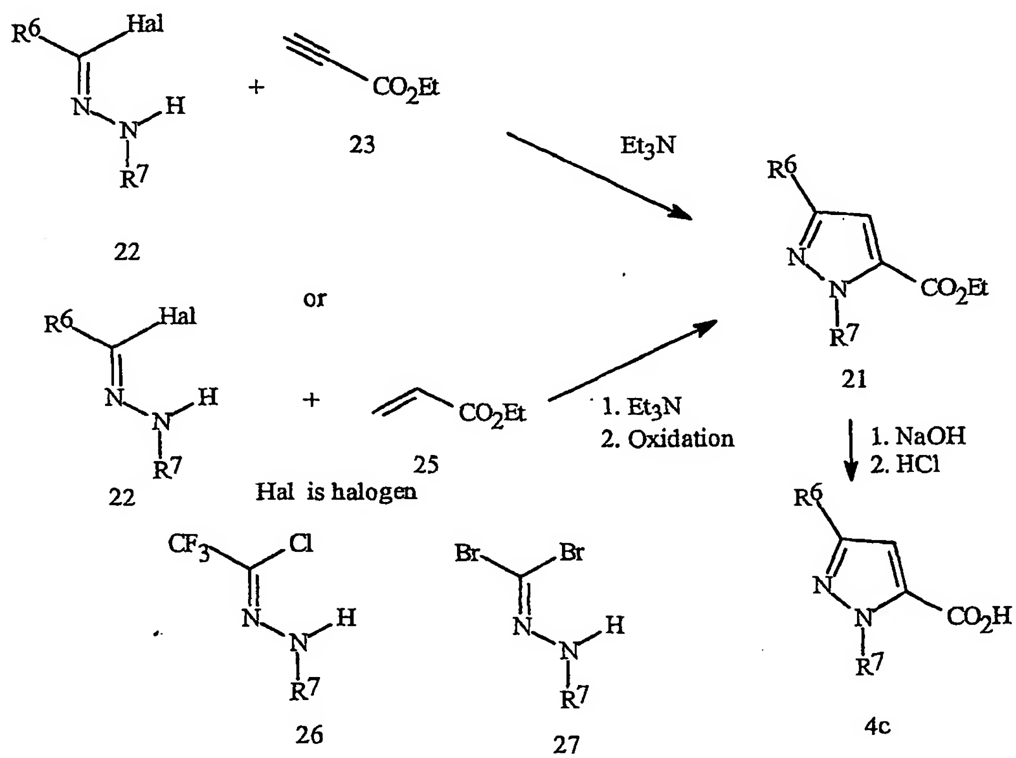
Scheme 14



Scheme 14 involves reaction of an optionally substituted phenyl hydrazine of Formula **19** with a ketopyruvate of Formula **20** to yield pyrazole esters of Formula **21**. Hydrolysis of the esters affords the pyrazole acids of Formula **4c**. This procedure is particularly useful for the preparation of compounds in which R^7 is optionally substituted phenyl and R^6 is haloalkyl.

An alternate synthesis of pyrazole acids of Formula **4c** is described in Scheme 15.

Scheme 15

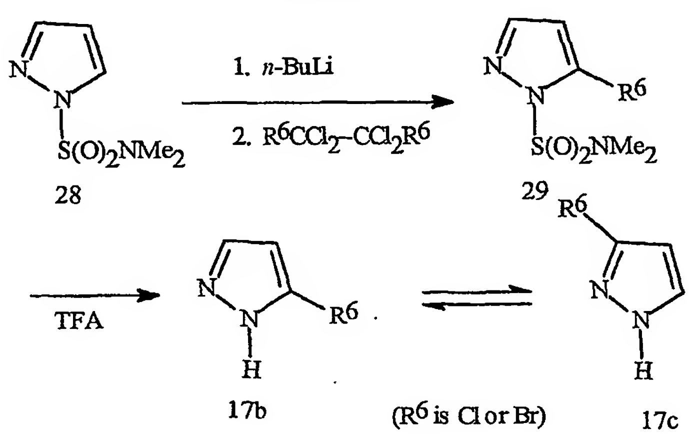


The method of Scheme 15 involves 3+2 cycloaddition of an appropriately substituted iminohalide **22** with either substituted propiolates of Formula **23** or acrylates of Formula **25**. Cycloaddition with an acrylate requires additional oxidation of the intermediate pyrazoline to the pyrazole. Hydrolysis of the esters affords the pyrazole acids of Formula **4c**. Preferred iminohalides for this reaction include the trifluoromethyl iminochloride of Formula **26** and the iminodibromide of Formula **27**. Compounds such as **26** are known (*J. Heterocycl. Chem.*

1985, *22*(2), 565-8). Compounds such as **27** are available by known methods (*Tetrahedron Letters* **1999**, *40*, 2605). These procedures are particularly useful for the preparation of compounds where R^7 is optionally substituted phenyl and R^6 is haloalkyl or bromo.

The starting pyrazoles of Formula **17** are known compounds or can be prepared according to known methods. The pyrazole of Formula **17a** (the compound of Formula **17** wherein R^6 is CF_3 and R^8 is H) can be prepared by literature procedures (*J. Fluorine Chem.* **1991**, *53*(1), 61-70). The pyrazoles of Formula **17c** (compounds of Formula **17** wherein R^6 is Cl or Br and R^8 is H) can also be prepared by literature procedures (*Chem. Ber.* **1966**, *99*(10), 3350-7). A useful alternative method for the preparation of compound **17c** is depicted in Scheme 16.

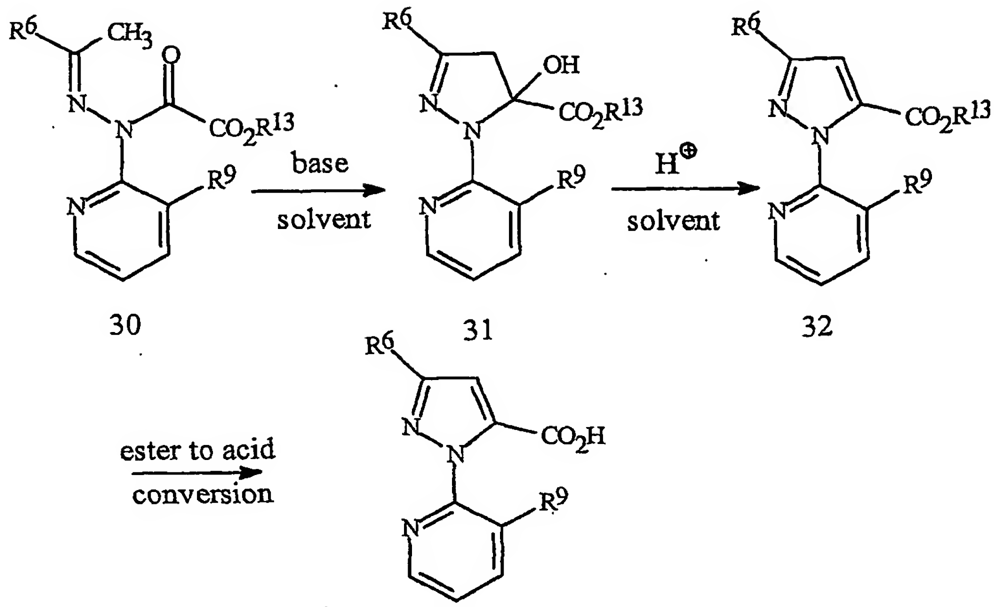
Scheme 16



In the method of Scheme 16, metallation of the sulfamoyl pyrazole of Formula **28** with *n*-butyllithium followed by direct halogenation of the anion with either hexachloroethane (for R^6 being Cl) or 1,2-dibromotetrachloroethane (for R^6 being Br) affords the halogenated derivatives of Formula **29**. Removal of the sulfamoyl group with trifluoroacetic acid (TFA) at room temperature proceeds cleanly and in good yield to afford the pyrazoles of Formula **17c**. One skilled in the art will recognize that Formula **17c** is a tautomer of Formula **17b**. Further experimental details for these procedures are described in Examples 8 and 10.

Pyrazolecarboxylic acids of Formula **4d** wherein R^6 is H, C_1-C_6 alkyl or C_1-C_6 haloalkyl can be prepared by the method outlined in Scheme 17.

Scheme 17



30 31 32 4d

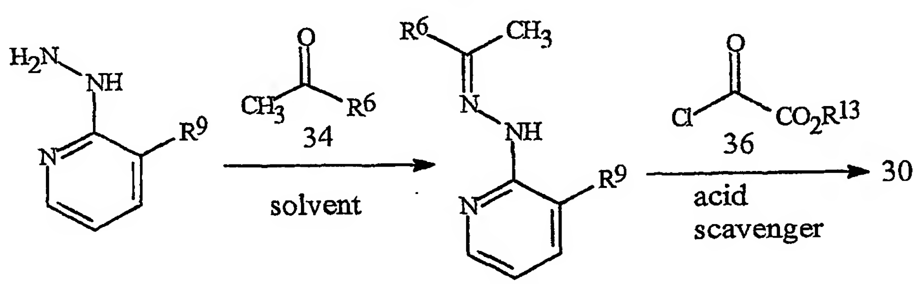
Reaction of a compound of Formula **30** wherein R^{13} is C_1–C_4 alkyl with a suitable base in a suitable organic solvent affords the cyclized product of Formula **31** after neutralization with an acid such as acetic acid. The suitable base can be, for example but not limitation, sodium hydride, potassium *t*-butoxide, dimsyl sodium ($CH_3S(O)CH_2^- Na^+$), alkali metal (such as lithium, sodium or potassium) carbonates or hydroxides, tetraalkyl (such as methyl, ethyl or butyl)ammonium fluorides or hydroxides, or 2-*tert*-butylimino-2-diethylamino-1,3-dimethyl-perhydro-1,3,2-diazaphosphonine. The suitable organic solvent can be, for example but not limitation, acetone, acetonitrile, tetrahydrofuran, dichloromethane, dimethylsulfoxide, or *N,N*-dimethylformamide. The cyclization reaction is usually conducted in a temperature range from about 0 to 120 °C. The effects of solvent, base, temperature and addition time are all interdependent, and choice of reaction conditions is important to minimize the formation of byproducts. A preferred base is tetrabutylammonium fluoride.

Dehydration of the compound of Formula **31** to give the compound of Formula **32**, followed by converting the carboxylic ester function to carboxylic acid, affords the compound of Formula **4d**. The dehydration is effected by treatment with a catalytic amount of a suitable acid. This catalytic acid can be, for example but not limitation, sulfuric acid. The reaction is generally conducted using an organic solvent. As one skilled in the art will realize, dehydration reactions may be conducted in a wide variety of solvents in a temperature range generally between about 0 and 200 °C, more preferably between about 0 and 100 °C. For the dehydration in the method of Scheme 17, a solvent comprising acetic acid and temperatures of about 65 °C are preferred. Carboxylic ester compounds can be converted to carboxylic acid compounds by numerous methods including nucleophilic

cleavage under anhydrous conditions or hydrolytic methods involving the use of either acids or bases (see T. W. Greene and P. G. M. Wuts, *Protective Groups in Organic Synthesis*, 2nd ed., John Wiley & Sons, Inc., New York, 1991, pp. 224–269 for a review of methods). For the method of Scheme 17, base-catalyzed hydrolytic methods are preferred. Suitable bases include alkali metal (such as lithium, sodium or potassium) hydroxides. For example, the ester can be dissolved in a mixture of water and an alcohol such as ethanol. Upon treatment with sodium hydroxide or potassium hydroxide, the ester is saponified to provide the sodium or potassium salt of the carboxylic acid. Acidification with a strong acid, such as hydrochloric acid or sulfuric acid, yields the carboxylic acid of Formula **4d**. The carboxylic acid can be isolated by methods known to those skilled in the art, including crystallization, extraction and distillation.

Compounds of Formula **30** can be prepared by the method outlined in Scheme 18.

Scheme 18



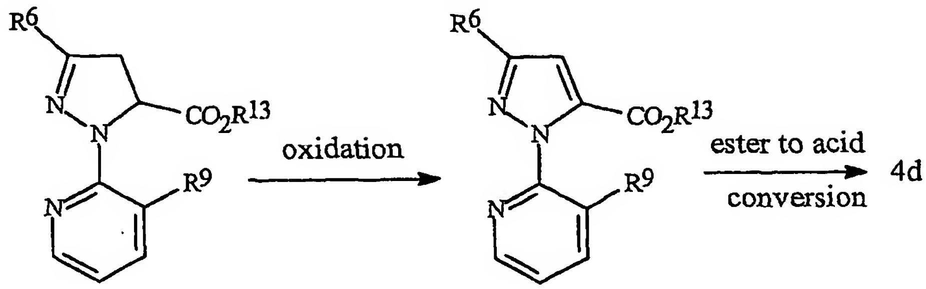
33 35

wherein R^6 is H, C_1-C_6 alkyl or C_1-C_6 haloalkyl and R^{13} is C_1–C_4 alkyl.

Treatment of a hydrazine compound of Formula **33** with a ketone of Formula **34** in a solvent such as water, methanol or acetic acid gives the hydrazone of Formula **35**. One skilled in the art will recognize that this reaction may require catalysis by an optional acid and may also require elevated temperatures depending on the molecular substitution pattern of the hydrazone of Formula **35**. Reaction of the hydrazone of Formula **35** with the compound of Formula **36** in a suitable organic solvent such as, for example but not limitation, dichloromethane or tetrahydrofuran in the presence of an acid scavenger such as triethylamine provides the compound of Formula **30**. The reaction is usually conducted at a temperature between about 0 and 100 °C. Further experimental details for the method of Scheme 18 are illustrated in Example 17. Hydrazine compounds of Formula **33** can be prepared by standard methods, such as by contacting the corresponding halo compound of Formula **15a** with hydrazine.

Pyrazolecarboxylic acids of Formula **4d** wherein R^6 is halogen can be prepared by the method outlined in Scheme 19.

Scheme 19



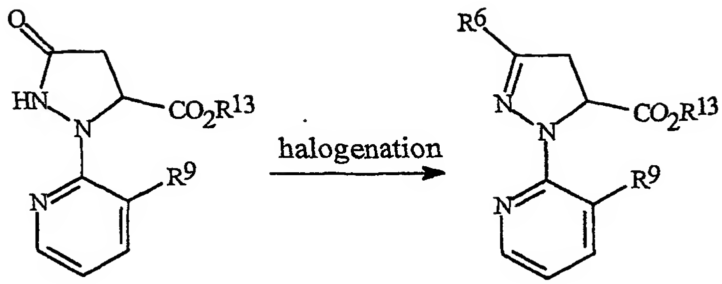
37 32

wherein R^{13} is C_1–C_4 alkyl.

Oxidization of the compound of Formula **37** optionally in the presence of acid to give the compound of Formula **32** followed by conversion of the carboxylic ester function to the carboxylic acid provides the compound of Formula **4d**. The oxidizing agent can be hydrogen peroxide, organic peroxides, potassium persulfate, sodium persulfate, ammonium persulfate, potassium monopersulfate (e.g., Oxone®) or potassium permanganate. To obtain complete conversion, at least one equivalent of oxidizing agent versus the compound of Formula **37** should be used, preferably between about one to two equivalents. This oxidation is typically carried out in the presence of a solvent. The solvent can be an ether, such as tetrahydrofuran, *p*-dioxane and the like, an organic ester, such as ethyl acetate, dimethyl carbonate and the like, or a polar aprotic organic such as *N,N*-dimethylformamide, acetonitrile and the like. Acids suitable for use in the oxidation step include inorganic acids, such as sulfuric acid, phosphoric acid and the like, and organic acids, such as acetic acid, benzoic acid and the like. The acid, when used, should be used in greater than 0.1 equivalents versus the compound of Formula **37**. To obtain complete conversion, one to five equivalents of acid can be used. The preferred oxidant is potassium persulfate and the oxidation is preferably carried out in the presence of sulfuric acid. The reaction can be carried out by mixing the compound of Formula **37** in the desired solvent and, if used, the acid. The oxidant can then be added at a convenient rate. The reaction temperature is typically varied from as low as about 0 °C up to the boiling point of the solvent in order to obtain a reasonable reaction time to complete the reaction, preferably less than 8 hours. The desired product, a compound of Formula **32** can be isolated by methods known to those skilled in the art, including crystallization, extraction and distillation. Methods suitable for converting the ester of Formula **32** to the carboxylic acid of Formula **4d** are already described for Scheme 17. Further experimental details for the method of Scheme 19 are illustrated in Examples 12 and 13.

Compounds of Formula **37** can be prepared from corresponding compounds of Formula **38** as shown in Scheme 20.

Scheme 20



38 37

wherein R^{13} is C_1–C_4 alkyl and R^6 is halogen.

Treatment of a compound of Formula **38** with a halogenating reagent, usually in the presence of a solvent, affords the corresponding halo compound of Formula **37**. Halogenating reagents that can be used include phosphorus oxyhalides, phosphorus trihalides, phosphorus pentahalides, thionyl chloride, dihalotrialkylphosphoranes, dihalodiphenylphosphoranes, oxalyl chloride and phosgene. Preferred are phosphorus oxyhalides and phosphorus pentahalides. To obtain complete conversion, at least 0.33 equivalents of phosphorus oxyhalide versus the compound of Formula **38** (i.e. the mole reatio of phosphorus oxyhalide to Formula **18** is at least 0.33) should be used, preferably between about 0.33 and 1.2 equivalents. To obtain complete conversion, at least 0.20 equivalents of phosphorus pentahalide versus the compound of Formula **38** should be used, preferably between about 0.20 and 1.0 equivalents. Compounds of Formula **38** wherein R^{13} is C_1–C_4 alkyl are preferred for this reaction. Typical solvents for this halogenation include halogenated alkanes, such as dichloromethane, chloroform, chlorobutane and the like, aromatic solvents, such as benzene, xylene, chlorobenzene and the like, ethers, such as tetrahydrofuran, *p*-dioxane, diethyl ether, and the like, and polar aprotic solvents such as acetonitrile, *N*,*N*-dimethylformamide, and the like. Optionally, an organic base, such as triethylamine, pyridine, *N*,*N*-dimethylaniline or the like, can be added. Addition of a catalyst, such as *N*,*N*-dimethylformamide, is also an option. Preferred is the process in which the solvent is acetonitrile and a base is absent. Typically, neither a base nor a catalyst is required when acetonitrile solvent is used. The preferred process is conducted by mixing the compound of Formula **38** in acetonitrile. The halogenating reagent is then added over a convenient time, and the mixture is then held at the desired temperature until the reaction is complete. The reaction temperature is typically between 20 °C and the boiling point of acetonitrile, and the reaction time is typically less than 2 hours. The reaction mass is then neutralized with an inorganic base, such as sodium bicarbonate, sodium hydroxide and the like, or an organic base, such as sodium acetate. The desired product, a compound of Formula **37**, can be

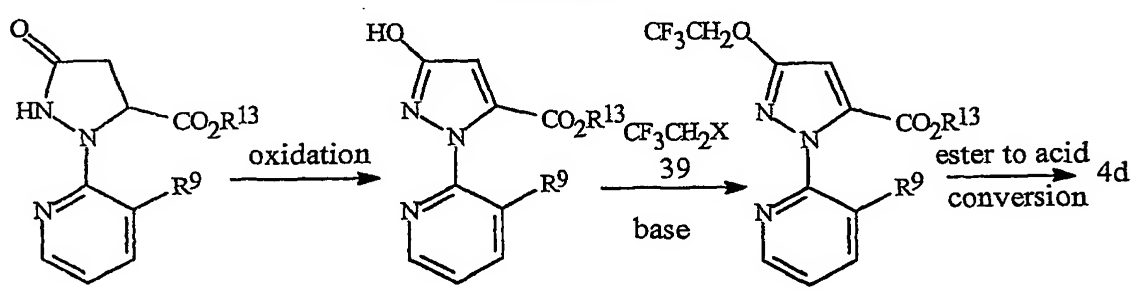
isolated by methods known to those skilled in the art, including crystallization, extraction and distillation.

Alternatively, compounds of Formula **37** wherein R^6 is halogen can be prepared by treating the corresponding compounds of Formula **37** wherein R^6 is a different halogen (e.g., Cl for making Formula **37** wherein R^3 is Br) or a sulfonate group such as *p*-toluenesulfonate, benzenesulfonate and methanesulfonate with the appropriate hydrogen halide. By this method the R^6 halogen or sulfonate substituent on the Formula **37** starting compound is replaced with, for example, Br or Cl from hydrogen bromide or hydrogen chloride, respectively. The reaction is conducted in a suitable solvent such as dibromomethane, dichloromethane or acetonitrile. The reaction can be conducted at or near atmospheric pressure or above atmospheric pressure in a pressure vessel. When R^6 in the starting compound of Formula **37** is a halogen such as Cl, the reaction is preferably conducted in such a way that the hydrogen halide generated from the reaction is removed by sparging or other suitable means. The reaction can be conducted between about 0 and 100 °C, most conveniently near ambient temperature (e.g., about 10 to 40 °C), and more preferably between about 20 and 30 °C. Addition of a Lewis acid catalyst (such as aluminum tribromide for preparing Formula **37** wherein R^6 is Br) can facilitate the reaction. The product of Formula **37** is isolated by the usual methods known to those skilled in the art, including extraction, distillation and crystallization. Further details for this process are illustrated in Example 14.

Starting compounds of Formula **37** wherein R^6 is Cl or Br can be prepared from corresponding compounds of Formula **38** as already described. Starting compounds of Formula **37** wherein R^6 is a sulfonate group can likewise be prepared from corresponding compounds of Formula **38** by standard methods such as treatment with a sulfonyl chloride (e.g., *p*-toluenesulfonyl chloride) and base such as a tertiary amine (e.g., triethylamine) in a suitable solvent such as dichloromethane; further details for this process are illustrated in Example 15.

Pyrazolecarboxylic acids of Formula **4d** wherein R^6 is C_1-C_4 alkoxy or C_1-C_4 haloalkoxy can also be prepared by the method outlined in Scheme 21.

Scheme 21



38 32a 32b

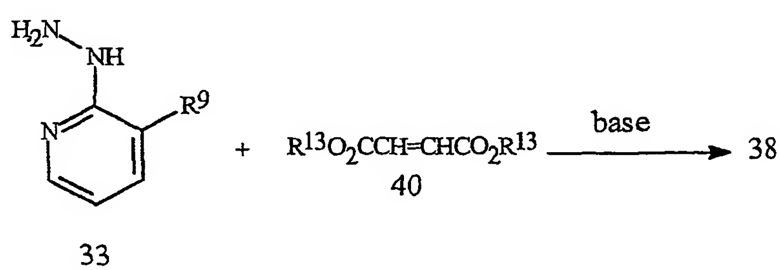
wherein R^{13} is C_1–C_4 alkyl, and X is a leaving group.

In this method, instead of being halogenated as shown in Scheme 20, the compound of Formula **38** is oxidized to the compound of Formula **32a**. The reaction conditions for this oxidation are as already described for the conversion of the compound of Formula **37** to the compound of Formula **32** in Scheme 19.

The compound of Formula **32a** is then alkylated to form the compound of Formula **32b** by contact with an alkylating agent CF_3CH_2X (**39**) in the presence of a base. In the alkylating agent **39**, X is a nucleophilic reaction leaving group such as halogen (e.g., Br, I), $OS(O)_2CH_3$ (methanesulfonate), $OS(O)_2CF_3$, $OS(O)_2Ph$-*p*-CH_3 (*p*-toluenesulfonate), and the like; methanesulfonate works well. The reaction is conducted in the presence of at least one equivalent of a base. Suitable bases include inorganic bases, such as alkali metal (such as lithium, sodium or potassium) carbonates and hydroxides, and organic bases, such as triethylamine, diisopropylethylamine and 1,8-diazabicyclo[5.4.0]undec-7-ene. The reaction is generally conducted in a solvent, which can comprise alcohols, such as methanol and ethanol, halogenated alkanes, such as dichloromethane, aromatic solvents, such as benzene, toluene and chlorobenzene, ethers, such as tetrahydrofuran, and polar aprotic solvents, such as acetonitrile, such as such as acetonitrile, *N,N*-dimethylformamide, and the like. Alcohols and polar aprotic solvents are preferred for use with inorganic bases. Potassium carbonate as base and acetonitrile as solvent are preferred. The reaction is generally conducted between about 0 and 150 °C, with most typically between ambient temperature and 100 °C. The product of Formula **32b** can be isolated by conventional techniques such as extraction. The ester of Formula **32b** can then be converted to the carboxylic acid of Formula **4d** by the methods already described for the conversion of Formula **32** to Formula **4d** in Scheme 17. Further experimental details for the method of Scheme 21 are illustrated in Example 16.

Compounds of Formula **38** can be prepared from compounds of Formula **33** as outlined in Scheme 22.

Scheme 22



wherein R^{13} is C_1–C_4 alkyl.

In this method, a hydrazine compound of Formula **33** is contacted with a compound of Formula **40** (a fumarate ester or maleate ester or a mixture thereof may be used) in the presence of a base and a solvent. The base is typically a metal alkoxide salt, such as sodium

methoxide, potassium methoxide, sodium ethoxide, potassium ethoxide, potassium *tert*-butoxide, lithium *tert*-butoxide, and the like. Greater than 0.5 equivalents of base versus the compound of Formula **33** should be used, preferably between 0.9 and 1.3 equivalents. Greater than 1.0 equivalents of the compound of Formula **40** should be used, preferably between 1.0 to 1.3 equivalents. Polar protic and polar aprotic organic solvents can be used, such as alcohols, acetonitrile, tetrahydrofuran, *N,N*-dimethylformamide, dimethyl sulfoxide and the like. Preferred solvents are alcohols such as methanol and ethanol. It is especially preferred that the alcohol be the same as that making up the fumarate or maleate ester and the alkoxide base. The reaction is typically conducted by mixing the compound of Formula **33** and the base in the solvent. The mixture can be heated or cooled to a desired temperature and the compound of Formula **40** added over a period of time. Typically reaction temperatures are between 0 °C and the boiling point of the solvent used. The reaction may be conducted under greater than atmospheric pressure in order to increase the boiling point of the solvent. Temperatures between about 30 and 90 °C are generally preferred. The addition time can be as quick as heat transfer allows. Typical addition times are between 1 minute and 2 hours. Optimum reaction temperature and addition time vary depending upon the identities of the compounds of Formula **33** and Formula **40**. After addition, the reaction mixture can be held for a time at the reaction temperature. Depending upon the reaction temperature, the required hold time may be from 0 to 2 hours. Typical hold times are 10 to 60 minutes. The reaction mass then can be acidified by adding an organic acid, such as acetic acid and the like, or an inorganic acid, such as hydrochloric acid, sulfuric acid and the like. Depending on the reaction conditions and the means of isolation, the $-CO_2R^{13}$ function on the compound of Formula **38** may be hydrolyzed to $-CO_2H$; for example, the presence of water in the reaction mixture can promote such hydrolysis. If the carboxylic acid ($-CO_2H$) is formed, it can be converted back to $-CO_2R^{13}$ wherein R^{13} is C_1–C_4 alkyl using esterification methods well-known in the art. The desired product, a compound of Formula **38**, can be isolated by methods known to those skilled in the art, such as crystallization, extraction or distillation.

It is recognized that some reagents and reaction conditions described above for preparing compounds of Formula **I** may not be compatible with certain functionalities present in the intermediates. In these instances, the incorporation of protection/deprotection sequences or functional group interconversions into the synthesis will aid in obtaining the desired products. The use and choice of the protecting groups will be apparent to one skilled in chemical synthesis (see, for example, Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; Wiley: New York, 1991). One skilled in the art will recognize that, in some cases, after the introduction of a given reagent as it is depicted in any individual scheme, it may be necessary to perform additional routine synthetic steps not described in detail to complete the synthesis of compounds of Formula **I**. One skilled in the

art will also recognize that it may be necessary to perform a combination of the steps illustrated in the above schemes in an order other than that implied by the particular sequence presented to prepare the compounds of Formula I.

It is believed that one skilled in the art using the preceding description can prepare compounds of Formula I of the present invention to its fullest extent. The following Examples are, therefore, to be construed as merely illustrative, and not limiting of the disclosure in any way whatsoever. Percentages are by weight except for chromatographic solvent mixtures or where otherwise indicated. Parts and percentages for chromatographic solvent mixtures are by volume unless otherwise indicated. ^{1}H NMR spectra are reported in ppm downfield from tetramethylsilane; s means singlet, d means doublet, t means triplet, q means quartet, m means multiplet, dd means doublet of doublets, dt means doublet of triplets, br s means broad singlet.

EXAMPLE 1

Preparation of 2-[1-Ethyl-3-trifluoromethylpyrazol-5-yl carbamoyl]-3-methyl-*N*-(1-methylethyl)benzamide

Step A: Preparation of 3-Methyl-*N*-(1-methylethyl)-2-nitrobenzamide

A solution of 3-methyl-2-nitrobenzoic acid (2.00 g, 11.0 mmol) and triethylamine (1.22 g, 12.1 mmol) in 25 mL of methylene chloride was cooled to 10 °C. Ethyl chloroformate was carefully added and a solid precipitate formed. After stirring for 30 minutes isopropylamine (0.94 g, 16.0 mmol) was added and a homogeneous solution resulted. The reaction was stirred for an additional hour, poured into water and extracted with ethyl acetate. The organic extracts were washed with water, dried over magnesium sulfate and evaporated under reduced pressure to afford 1.96 g of the desired intermediate as a white solid melting at 126-128 °C.

^{1}H NMR ($CDCl_3$) δ 1.24 (d, 6H), 2.38 (s, 3H), 4.22 (m, 1H), 5.80 (br s, 1H), 7.4 (m, 3H).

Step B: Preparation of 2-Amino-3-methyl-*N*-(1-methylethyl)benzamide

The 2-nitrobenzamide of Step A (1.70 g, 7.6 mmol) was hydrogenated over 5% Pd/C in 40 mL of ethanol at 50 psi. When the uptake of hydrogen ceased the reaction was filtered through Celite® diatomaceous filter aid and the Celite® was washed with ether. The filtrate was evaporated under reduced pressure to afford 1.41 g of the title compound as a solid melting at 149-151 °C.

^{1}H NMR ($CDCl_3$) δ 1.24 (dd, 6H), 2.16 (s, 3H), 4.25 (m, 1H), 5.54 (br s, 2H), 5.85 (br s, 1H), 6.59 (t, 1H), 7.13 (d, 1H), 7.17 (d, 1H).

Step C: Preparation of 1-Ethyl-3-trifluoromethylpyrazol-5-yl carboxylic acid

To a mixture of 3-trifluoromethylpyrazole (5 g, 37 mmol) and powdered potassium carbonate (10 g, 72 mmol) stirring in 30 mL of *N,N*-dimethylformamide, iodoethane (8 g,

51 mmol) was added dropwise. After a mild exotherm, the reaction was stirred overnight at room temperature. The reaction mixture was partitioned between 100 mL of diethyl ether and 100 mL of water. The ether layer was separated, washed with water (3X) and brine, and dried over magnesium sulfate. Evaporation of solvent *in vacuo* gave 4 g of oil.

To 3.8 g of this oil stirring in 40 mL of tetrahydrofuran under nitrogen in a dry ice/acetone bath, 17 mL of a 2.5 M solution of *n*-butyllithium in tetrahydrofuran (43 mmol) was added dropwise and the solution stirred for 20 minutes at -78 °C. An excess of gaseous carbon dioxide was bubbled into the stirred solution at a moderate rate for 10 minutes. After addition of carbon dioxide, the reaction was allowed to slowly reach room temperature and stirred overnight. The reaction mixture was partitioned between diethyl ether (100 mL) and 0.5 N aqueous sodium hydroxide (100 mL). The basic layer was separated and acidified with concentrated hydrochloric acid to a pH of 2-3. The aqueous mixture was extracted with ethyl acetate (100 mL) and the organic extract washed with water and brine and dried over magnesium sulfate. The oily residue, which remained after evaporating the solvent *in vacuo*, was triturated to a solid from a small amount of 1-chlorobutane. After filtering and drying, a slightly impure sample of 1-ethyl-3-trifluoromethyl-pyrazol-5-yl carboxylic acid (1.4 g) was obtained as a broad-melting solid.

^{1}H NMR ($CDCl_3$) δ 1.51 (t, 3H), 4.68 (q, 2H), 7.23 (s, 1H), 9.85 (br s, 1H).

Step D: <u>Preparation of 2-[1-Ethyl-3-trifluoromethylpyrazol-5-yl carbamoyl]-3-methyl-*N*-(1-methylethyl)benzamide</u>

To a solution of 1-ethyl-3-trifluoromethyl-pyrazol-5-yl carboxylic acid (i.e. the product of Step C) (0.5 g, 2.4 mmol) stirring in 20 mL of methylene chloride, oxalyl chloride (1.2 mL, 14 mmol) was added. Upon addition of 2 drops of *N,N*-dimethylformamide, foaming and bubbling occurred. The reaction mixture was heated at reflux for 1 hr as a yellow solution. After cooling, the solvent was removed *in vacuo* and the resulting residue dissolved in 20 mL of tetrahydrofuran. To the stirred solution, 2-amino-3-methyl-*N*-(1-methylethyl)benzamide (i.e. the product of Step B) (0.7 g, 3.6 mmol) was added followed by the dropwise addition of *N,N*-diisopropylethylamine (3 mL, 17 mmol). After stirring at room temperature overnight, the reaction mixture was partitioned between ethyl acetate (100 mL) and 1*N* aqueous hydrochloric acid (75 mL). The separated organic layer was washed with water and brine and dried over magnesium sulfate. Evaporating *in vacuo* gave a white solid residue, which on purification by flash column chromatography on silica gel (2:1 hexanes/ethyl acetate) afforded 0.5 g of the title compound, a compound of the present invention, melting at 223-226 °C.

^{1}H NMR (DMSO-d_6) δ 1.06 (d, 6H), 1.36 (t, 3H), 2.45 (s, 3H), 3.97 (m, 1H), 4.58 (q, 2H), 7.43-7.25 (m, 3H), 7.45 (s, 1H), 8.05 (d, 1H), 10.15 (s, 1H).

EXAMPLE 2

Preparation of *N*-[2-Methyl-6-[[(1-methylethyl)amino]carbonyl]phenyl]-1-phenyl-3-(trifluoromethyl)-1H-pyrazole-5-carboxamide

Step A: Preparation of 2-Methyl-1-phenyl-4-(trifluoromethyl)-1*H*-pyrazole

A solution of 1,1,1-trifluoropentane-2,4-dione (20.0 g, 0.130 mole) in glacial acetic acid (60 mL) was cooled to 7 °C using an ice/water bath. Phenylhydrazine (14.1 g, 0.130 mole) was added dropwise over a period of 60 minutes. The reaction mass temperature increased to 15 °C during the addition. The resulting orange solution was held under ambient conditions for 60 minutes. The bulk of the acetic acid was removed by stripping on a rotary evaporator at a bath temperature of 65 °C. The residue was dissolved in methylene chloride (150 mL). The solution was washed with aqueous sodium bicarbonate (3 g in 50 mL of water). The purple-red organic layer was separated, treated with activated charcoal (2 g) and $MgSO_4$, then filtered. Volatiles were removed on a rotary evaporator. The crude product consisted of 28.0 g of a rose-colored oil, which contained ~89% the desired product and 11% 1-phenyl-5-(trifluoromethyl)-3-methylpyrazole.

^{1}H NMR (DMSO-d_6) δ 2.35 (s, 3H), 6.76 (s, 1H), 7.6-7.5 (m, 5H).

Step B: Preparation of 1-Phenyl-3-(trifluoromethyl)-1*H*-pyrazole-5-carboxylic acid

A sample of crude 2-methyl-1-phenyl-4-(trifluoromethyl)-1*H*-pyrazole (i.e. the product of Step A) (~89%, 50.0 g, 0.221 mole) was mixed with water (400 mL) and cetyltrimethylammonium chloride (4.00 g, 0.011 mole). The mixture was heated to 95 °C. Potassium permanganate was added in 10 equal portions, spaced at ~8 minute intervals. The reaction mass was maintained at 95-100 °C during this period. After the last portion was added, the mixture was held for ~15 minutes at 95-100 °C, whereupon the purple, permanganate color had been discharged. The reaction mass was filtered while hot (~75 °C) through a 1-cm bed of Celite® diatomaceous filter aid in a 150-mL coarse glass frit funnel. The filter cake was washed with warm (~50 °C) water (3x100mL). The combined filtrate and washings were extracted with ether (2x100 mL) to remove a small amount of yellow, water-insoluble material. The aqueous layer was purged with nitrogen to remove residual ether. The clear, colorless alkaline solution was acidified by adding concentrated hydrochloric acid dropwise until the pH reached ~1.3 (28 g, 0.28 mole). Gas evolution was vigorous during the first two-thirds of the addition. The product was collected via filtration, washed with water (3x40 mL), then dried overnight at 55 °C *in vacuo*. The product consisted of 11.7 g of a white, crystalline powder, which was essentially pure based upon ^{1}H NMR.

^{1}H NMR ($CDCl_3$) δ 7.33 (s, 1H), 7.4-7.5 (m, 5H).

Step C: Preparation of 1-Phenyl-3-(trifluoromethyl)-1*H*-pyrazole-5-carbonyl chloride

A sample of crude 1-phenyl-3-(trifluoromethyl)pyrazole-5-carboxylic acid (i.e. the product of Step B) (4.13 g, 16.1 mmol) was dissolved in methylene chloride (45 mL). The solution was treated with oxalyl chloride (1.80 mL, 20.6 mmol), followed by *N,N*-dimethylformamide (0.010 mL, 0.13 mmol). Off-gassing began shortly after adding the *N,N*-dimethylformamide catalyst. The reaction mixture was stirred for ~20 minutes under ambient conditions, then was heated to reflux for a period of 35 minutes. Volatiles were removed by stripping the reaction mixture on a rotary evaporator at a bath temperature of 55 °C. The product consisted of 4.43 g of a light-yellow oil. The only impurity observed by ^{1}H NMR was *N,N*-dimethylformamide.

^{1}H NMR ($CDCl_3$) δ 7.40 (m, 1H), 7.42 (s, 1H), 7.50-7.53 (m, 4H).

Step D: Preparation of *N*-[2-Methyl-6-[[(1-methylethyl)amino]carbonyl]phenyl]-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole-5-carboxamide

A sample of 3-methylisatoic anhydride (0.30 g, 1.7 mmol) partially dissolved in pyridine (4.0 mL) was treated with 1-phenyl-3-(trifluoromethylpyrazole)-5-carboxyl chloride (i.e. the product of Step C) (0.55 g, 1.9 mmol). The mixture was heated to ~95°C for a period of 2 hours. The resulting orange solution was cooled to 29 °C, then was treated with isopropylamine (1.00 g, 16.9 mmol). The reaction mass exothermically warmed to 39 °C. It was further heated to 55 °C for a period of 30 minutes, whereupon much precipitate formed. The reaction mass was dissolved in dichloromethane (150 mL). The solution was washed with aqueous acid (5 mL of conc. HCl in 45 mL of water), then with aqueous base (2 g sodium carbonate in 50 mL of water). The organic layer was dried over $MgSO_4$, filtered, then concentrated on a rotary evaporator. Upon reduction to ~4 mL, product crystals had formed. The slurry was diluted with ~10 mL of ether, whereupon more product precipitated. The product was isolated by filtration, washed with ether (2x10 mL), then washed with water (2x50 mL). The wet cake was dried for 30 minutes at 70 °C *in vacuo*. The product, a compound of the present invention, consisted of 0.52 g of an off-white powder melting at 260-262 °C.

^{1}H NMR (DMSO-d_6) δ 1.07 (d, 6H), 2.21 (s, 3H), 4.02 (octet, 1H), 7.2-7.4 (m, 3H), 7.45-7.6 (m, 6H), 8.10 (d, 1H), 10.31 (s, 1H).

EXAMPLE 3

Preparation of *N*-[2-Methyl-6-[[(1-methylethyl)amino]carbonyl]phenyl]-3-(trifluoromethyl)-1-[3-(trifluoromethyl)-2-pyridinyl]-1*H*-pyrazole-5-carboxamide

Step A: Preparation of 3-Trifluoromethyl-2-[3-(trifluoromethyl)-1*H*-pyrazol-1-yl]pyridine

A mixture of 2-chloro-3-trifluoromethylpyridine (3.62 g., 21 mmol), 3-trifluoromethylpyrazole (2.7 g., 20 mmol), and potassium carbonate (6.0 g, 43 mmol) were heated at 100 °C for 18 h. The cooled reaction mixture was added to ice/water (100 mL). The mixture was extracted twice with ether (100 mL) and the combined ether extracts were washed twice with water (100 mL). The organic layer was dried with magnesium sulfate and concentrated to an oil. Chromatography on silica gel with hexanes:ethyl acetate (8:1 to 4:1) as eluent gave the title compound (3.5 g) as an oil.

^{1}H NMR ($CDCl_3$) δ 6.75 (m, 1H), 7.5 (m, 1H), 8.2 (m, 2H), 8.7 (m, 1H).

Step B: Preparation of 3-(Trifluoromethyl)-1-[3-(trifluoromethyl)-2-pyridinyl]-1*H*-pyrazole-5-carboxylic acid

A mixture of the title compound of Example 3, Step A (3.4 g, 13 mmol) was dissolved in tetrahydrofuran (30 mL) and cooled to -70 °C. Lithium diisopropylamide (2*N* in heptane/tetrahydrofuran, (Aldrich) 9.5 mL, 19 mmol) was added and the resulting dark mixture was stirred for 10 minutes. Dry carbon dioxide was bubbled through the mixture for 15 minutes. The mixture was allowed to warm to 23 °C and treated with water (50 mL) and 1*N* sodium hydroxide (10 mL). The aqueous mixture was extracted with ether (100 mL) and then ethyl acetate (100 mL). The aqueous layer was acidified with 6*N* hydrochloric acid to pH 1-2 and extracted twice with dichloromethane. The organic layer was dried with magnesium sulfate and concentrated to give the title compound (1.5 g).

^{1}H NMR ($CDCl_3$) δ 7.6 (m, 1H), 7.95 (m, 1H), 8.56 (m, 1H), 8.9 (m, 1H), 14.2 (br, 1H)

Step C: Preparation of *N*-[2-Methyl-6-[[(1-methylethyl)amino]carbonyl]phenyl]-3-(trifluoromethyl)-1-[3-(trifluoromethyl)-2-pyridinyl]-1*H*-pyrazole-5-carboxamide

A mixture of the title compound of Example 3, Step B (0.54 g, 1.1 mmol), the title compound from Example 1, Step B (0.44 g, 2.4 mmol) and BOP chloride (bis(2-oxo-oxazolidinyl)phosphinyl chloride, 0.54 g, 2.1 mmol) in acetonitrile (13 mL) was treated with triethylamine (0.9 mL). The mixture was shaken in a closed scintillation vial for 18 h. The reaction was partitioned between ethyl acetate (100 mL) and 1*N* hydrochloric acid. The ethyl acetate layer was washed successively with 1*N* hydrochloric acid (50 mL), 1*N* sodium hydroxide (50 mL) and saturated sodium chloride solution (50 mL). The organic layer was dried over magnesium sulfate and concentrated. The residue was subjected to column

chromatography on silica gel with hexanes/ethyl acetate (5:1 to 3:1) as eluent. The title compound (0.43 g), a compound of the present invention, was isolated as a white solid. m.p. 227-230 °C.

^{1}H NMR ($CDCl_3$) δ 1.2 (m, 6H), 4.15 (m, 1H), 5.9 (br d, 1H), 7.1 (m, 1H), 7.2 (m, 2H), 7.4 (s, 1H), 7.6 (m, 1H), 8.15 (m, 1H), 8.74 (m, 1H), 10.4 (br, 1H).

EXAMPLE 4

Preparation of 1-(3-Chloro-2-pyridinyl)-*N*-[2-methyl-6-[[(1-methylethyl)amino]carbonyl]-phenyl]-3-(trifluoromethyl)-1*H*-pyrazole-5-carboxamide

Step A: Preparation of 3-Chloro-2-[3-(trifluoromethyl)-1*H*-pyrazol-1-yl]pyridine

To a mixture of 2,3-dichloropyridine (99.0 g, 0.67 mol) and 3-(trifluoromethyl)-pyrazole (83 g, 0.61 mol) in dry *N,N*-dimethylformamide (300 mL) was added potassium carbonate (166.0 g, 1.2 mol) and the reaction was then heated to 110-125 °C over 48 hours. The reaction was cooled to 100 °C and filtered through Celite® diatomaceous filter aid to remove solids. *N,N*-Dimethylformamide and excess dichloropyridine were removed by distillation at atmospheric pressure. Distillation of the product at reduced pressure (b.p. 139-141 °C, 7 mm) afforded the desired intermediate as a clear yellow oil (113.4 g).

^{1}H NMR ($CDCl_3$) δ 6.78 (s, 1H), 7.36 (t, 1H), 7.93 (d, 1H), 8.15 (s, 1H), 8.45 (d, 1H).

Step B: Preparation of 1-(3-Chloro-2-pyridinyl)-3-(trifluoromethyl)-1*H*-pyrazole-5-carboxylic acid

To a solution of 3-chloro-2-[3-(trifluoromethyl)-1*H*-pyrazol-1-yl]pyridine (i.e. the product of Step A) (105.0 g, 425 mmol) in dry tetrahydrofuran (700 mL) at -75 °C was added via cannula a -30 °C solution of lithium diisopropylamide (425 mmol) in dry tetrahydrofuran (300 mL). The deep red solution was stirred for 15 minutes, after which time carbon dioxide was bubbled through at -63 °C until the solution became pale yellow and the exothermicity ceased. The reaction was stirred for an additional 20 minutes and then quenched with water (20 mL). The solvent was removed under reduced pressure, and the reaction mixture partitioned between ether and 0.5*N* aqueous sodium hydroxide solution. The aqueous extracts were washed with ether (3x), filtered through Celite® diatomaceous filter aid to remove residual solids, and then acidified to a pH of approximately 4, at which point an orange oil formed. The aqueous mixture was stirred vigorously and additional acid was added to lower the pH to 2.5-3. The orange oil congealed into a granular solid, which was filtered, washed successively with water and 1*N* hydrochloric acid, and dried under vacuum at 50 °C to afford the title product as an off-white solid (130 g). (Product from another run following similar procedures melted at 175-176 °C.)

^{1}H NMR (DMSO-d_6) δ 7.61 (s, 1H), 7.76 (dd, 1H), 8.31 (d, 1H), 8.60 (d, 1H).

Step C: Preparation of 8-Methyl-2*H*-3,1-benzoxazine-2,4(1*H*)-dione

To a solution of 2-amino-3-methylbenzoic acid (6 g) in dry 1,4-dioxane (50 mL) was added dropwise a solution of trichloromethyl chloroformate (8 mL) in dry 1,4-dioxane (25 mL), with ice-water cooling to keep the reaction temperature below 25 °C. A white precipitate began to form during the addition. The reaction mixture was stirred at room temperature overnight. The precipitated solids were removed by filtration and washed with 1,4-dioxane (2x20 mL) and hexane (2x15 mL) and air-dried to yield 6.51 g of off-white solid.

^{1}H NMR (DMSO-d_6) δ 2.33 (s, 3H), 7.18 (t, 1H), 7.59 (d, 1H), 7.78 (d, 1H), 11.0 (br s, 1H).

Step D: Preparation of 2-[1-(3-Chloro-2-pyridinyl)-3-(trifluoromethyl)-1*H*-pyrazol-5-yl]-8-methyl-4*H*-3,1-benzoxazin-4-one

To a suspension of the carboxylic acid product prepared as in Step B (146 g, 500 mmol) in dichloromethane (approximately 2 L) was added *N,N*-dimethylformamide (20 drops) and oxalyl chloride (67 mL, 750 mmol) in approximately 5-mL portions over approximately 2 h. Vigorous gas evolution occurred during the addition. The reaction mixture was stirred at room temperature overnight. The reaction mixture was concentrated *in vacuo* to provide the crude acid chloride as an opaque orange mixture. This material was taken up in dichloromethane, filtered to remove some solids and then reconcentrated and used without further purification. The crude acid chloride was dissolved in acetonitrile (250 mL) and added to a suspension of the product from Step C in acetonitrile (400 mL). Pyridine (250 mL) was added, the mixture was stirred for 15 min at room temperature, then warmed to reflux for 3 h. The resulting mixture was cooled to room temperature and stirred overnight to provide a solid mass. Additional acetonitrile was added and the mixture was mixed to form a thick slurry. The solids were collected and washed with cold acetonitrile. The solids were air-dried and the dried *in vacuo* at 90 °C for 5 h to yield 144.8 g of fluffy white solid.

^{1}H NMR ($CDCl_3$) δ 1.84 (s, 3H), 7.4 (t, 1H), 7.6 (m, 3H), 8.0 (dd, 1H), 8.1 (s, 1H), 8.6 (d, 1H).

Step E: Preparation of 1-(3-Chloro-2-pyridinyl)-*N*-[2-methyl-6-[[(1-methylethyl)-amino]carbonyl]phenyl]-3-(trifluoromethyl)-1*H*-pyrazole-5-carboxamide

To a suspension of the benzoxazinone product of Step D (124 g, 300 mmol) in dichloromethane (500 mL) was added dropwise isopropylamine (76 mL, 900 mmol) at room temperature. The temperature of the reaction mixture rose and the suspension thinned during the addition. The reaction mixture was then warmed to reflux for 1.5 h. A new suspension formed. The reaction mixture was cooled to room temperature and diethyl ether (1.3 L) was added and the mixture stirred at room temperature overnight. The solids were collected and washed with ether. The solids were air-dried and then dried *in vacuo* at 90 °C for 5 h to

yield 122 g of the title compound, a compound of the present invention, as a fluffy white solid, melting at 194-196 °C.

^{1}H NMR ($CDCl_3$) δ 1.23 (d, 6H), 2.21 (s, 3H), 4.2 (m, 1H), 5.9 (d, 1H), 7.2 (t, 1H), 7.3 (m, 2H), 7.31 (s, 1H), 7.4 (m, 1H), 7.8 (d, 1H), 8.5 (d, 1H), 10.4 (s, 1H).

EXAMPLE 5

Alternate preparation of 1-(3-chloro-2-pyridinyl)-*N*-[2-methyl-6-[[(1-methylethyl)amino]-carbonyl]phenyl]-3-(trifluoromethyl)-1*H*-pyrazole-5-carboxamide

To a solution of the carboxylic acid product prepared as in Example 4, Step B (28 g, 96 mmol) in dichloromethane (240 mL) was added *N,N*-dimethylformamide (12 drops) and oxalyl chloride (15.8 g, 124 mmol). The reaction mixture was stirred at room temperature until gas evolution ceased (approximately 1.5 h). The reaction mixture was concentrated *in vacuo* to provide the crude acid chloride as an oil that was used without further purification. The crude acid chloride was dissolved in acetonitrile (95 mL) and added to a solution of the benzoxazin-2,4-dione prepared as in Example 4, Step C in acetonitrile (95 mL). The resulting mixture was stirred at room temperature (approximately 30 min). Pyridine (95 mL) was added and the mixture heated to about 90 °C (approximately 1 h). The reaction mixture was cooled to about 35 °C and isopropylamine (25 mL) was added. The reaction mixture exothermically warmed during the addition and then was maintained at about 50 °C (approximately 1 h). The reaction mixture was then poured into ice water and stirred. The resulting precipitate was collected by filtration, washed with water and dried *in vacuo* overnight to provide 37.5 g of the title compound, a compound of the present invention, as a tan solid.

^{1}H NMR ($CDCl_3$) δ 1.23 (d, 6H), 2.21 (s, 3H), 4.2 (m, 1H), 5.9 (d, 1H), 7.2 (t, 1H), 7.3 (m, 2H), 7.31 (s, 1H), 7.4 (m, 1H), 7.8 (d, 1H), 8.5 (d, 1H), 10.4 (s, 1H).

EXAMPLE 6

Preparation of *N*-[4-chloro-2-methyl-6-[[(1-methylethyl)amino]carbonyl]phenyl]-1-(3-chloro-2-pyridinyl)-3-(trifluoromethyl)-1*H*-pyrazole-5-carboxamide

Step A: Preparation of 2-Amino-3-methyl-5-chlorobenzoic acid

To a solution of 2-amino-3-methylbenzoic acid (Aldrich, 15.0 g, 99.2 mmol) in *N,N*-dimethylformamide (50 mL) was added *N*-chlorosuccinimide (13.3 g, 99.2 mmol) and the reaction mixture was heated to 100 °C for 30 minutes. The heat was removed, the reaction was cooled to room temperature and let stand overnight. The reaction mixture was then slowly poured into ice-water (250 mL) to precipitate a white solid. The solid was filtered and washed four times with water and then taken up in ethyl acetate (900 mL). The ethyl acetate solution was dried over magnesium sulfate, evaporated under reduced pressure

and the residual solid was washed with ether to afford the desired intermediate as a white solid (13.9 g).

^{1}H NMR (DMSO-d_6) δ 2.11 (s, 3H), 7.22 (s, 1H), 7.55 (s, 1H).

Step B: Preparation of 3-chloro-2-[3-(trifluoromethyl)-1*H*-pyrazol-1-yl]pyridine

To a mixture of 2,3-dichloropyridine (99.0 g, 0.67 mol) and 3-trifluoromethyl pyrazole (83 g, 0.61 mol) in dry *N,N*-dimethylformamide (300 mL) was added potassium carbonate (166.0 g, 1.2 mol) and the reaction was then heated to 110-125 °C over 48 hours. The reaction was cooled to 100 °C and filtered through Celite® diatomaceous filter aid to remove solids. *N,N*-Dimethylformamide and excess dichloropyridine were removed by distillation at atomospheric pressure. Distillation of the product at reduced pressure (b.p. 139-141 °C, 7 mm) afforded the title compound as a clear yellow oil (113.4 g).

^{1}H NMR ($CDCl_3$) δ 6.78 (s, 1H), 7.36 (t, 1H), 7.93 (d, 1H), 8.15 (s, 1H), 8.45 (d, 1H).

Step C: Preparation of 1-(3-Chloro-2-pyridinyl)-3-(trifluoromethyl)-1*H*-pyrazole-5-carboxylic acid

To a solution of the pyrazole product from Step B (105.0 g, 425 mmol) in dry tetrahydrofuran (700 mL) at -75 °C was added via cannula a -30 °C solution of lithium diisopropylamide (425 mmol) in dry tetrahydrofuran (300 mL). The deep red solution was stirred for 15 minutes, after which time carbon dioxide was bubbled through at -63 °C until the solution became pale yellow and the exothermicity ceased. The reaction was stirred for an additional 20 minutes and then quenched with water (20 mL). The solvent was removed under reduced pressure, and the reaction mixture was partitioned between ether and 0.5 N aqueous sodium hydroxide solution. The aqueous extracts were washed with ether (3x), filtered through Celite® diatomaceous filter aid to remove residual solids, and then acidified to a pH of approximately 4, at which point an orange oil formed. The aqueous mixture was stirred vigorously and additional acid was added to lower the pH to 2.5-3. The orange oil congealed into a granular solid, which was filtered, washed successively with water and 1N hydrochloric acid, and dried under vacuum at 50 °C to afford the title product as an off-white solid (130 g). (Product from another run following similar procedure melted at 175-176 °C.)

^{1}H NMR (DMSO-d_6) δ 7.61 (s, 1H), 7.76 (dd, 1H), 8.31 (d, 1H), 8.60 (d, 1H).

Step D: Preparation of 6-chloro-2-[1-(3-chloro-2-pyridinyl)-3-(trifluoromethyl)-1*H*-pyrazol-5-yl]-8-methyl-4*H*-3,1-benzoxazin-4-one

To a solution of methanesulfonyl chloride (2.2 mL, 28.3 mmol) in acetonitrile (75 mL) was added dropwise a mixture of the carboxylic acid product from Step C (7.5 g, 27.0 mmol) and triethylamine (3.75 mL, 27.0 mmol) in acetonitrile (75 mL) at 0-5 °C. The reaction temperature was then maintained at 0 °C throughout successive addition of reagents. After stirring for 20 minutes, 2-amino-3-methyl-5-chlorobenzoic acid from Step A (5.1 g, 27.0 mmol) was added and stirring was continued for an additional 5 minutes. A solution of

triethylamine (7.5 mL, 54.0 mmol) in acetonitrile (15 mL) was then added dropwise, and the reaction mixture was stirred 45 minutes, followed by the addition of methanesulfonyl chloride (2.2 mL, 28.3 mmol). The reaction mixture was then warmed to room temperature and stirred overnight. Approximately 75 mL of water was then added to precipitate 5.8 g of a yellow solid. An additional 1 g of product was isolated by extraction from the filtrate to provide a total of 6.8 g of the title compound as a yellow solid.

^{1}H NMR ($CDCl_3$) δ 1.83 (s, 3H), 7.50 (s, 1H), 7.53 (m, 2H), 7.99 (m, 2H), 8.58 (d, 1H).

Step E: Preparation of *N*-[4-Chloro-2-methyl-6-[[(1-methylethyl)amino]carbonyl]-phenyl]-1-(3-chloro-2-pyridinyl)-3-(trifluoromethyl)-1*H*-pyrazole-5-carboxamide

To a solution of the benzoxazinone product of Step D (5.0 g, 11.3 mmol) in tetrahydrofuran (35 mL) was added dropwise isopropylamine (2.9 mL, 34.0 mmol) in tetrahydrofuran (10 mL) at room temperature. The reaction mixture was then warmed until all solids had dissolved and stirred an additional five minutes, at which point thin layer chromatography on silica gel confirmed completion of the reaction. The tetrahydrofuran solvent was evaporated under reduced pressure, and the residual solid was purified by chromatography on silica gel, followed by trituration with ether/hexane to afford the title compound, a compound of the present invention, as a solid (4.6 g), melting at 195-196 °C.

^{1}H NMR ($CDCl_3$) δ 1.21 (d, 6H), 2.17 (s, 3H), 4.16 (m, 1H), 5.95 (br d, 1H), 7.1-7.3 (m, 2H), 7.39 (s, 1H), 7.4 (m, 1H), 7.84 (d, 1H), 8.50 (d, 1H), 10.24 (br s, 1H).

EXAMPLE 7

Preparation of *N*-[4-Chloro-2-methyl-6-[(methylamino)carbonyl]phenyl]-1-(3-chloro-2-pyridinyl)-3-(trifluoromethyl)-1*H*-pyrazole-5-carboxamide

To a solution of the benzoxazinone product of Example 6, Step D (4.50 g, 10.18 mmol) in tetrahydrofuran (THF; 70 mL) was added methylamine (2.0 M solution in THF, 15 mL, 30.0 mmol) dropwise and the reaction mixture was stirred at room temperature for 5 minutes. The tetrahydrofuran solvent was evaporated under reduced pressure and the residual solid was purified by chromatography on silica gel to afford 4.09 g of the title compound, a compound of the present invention, as a white solid melting at 185-186 °C.

^{1}H NMR (DMSO-d_6) δ 2.17 (s, 3H), 2.65 (d, 3H), 7.35 (d, 1H), 7.46 (dd, 1H), 7.65 (dd, 1H), 7.74 (s, 1H), 8.21 (d, 1H), 8.35 (br q, 1H), 8.74 (d, 1H), 10.39 (s, 1H).

EXAMPLE 8

Preparation of 3-Chloro-*N*-[4-chloro-2-methyl-6-[[(1-methylethyl)amino]carbonyl]phenyl]-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxamide

Step A: Preparation of 3-Chloro-*N*,*N*-dimethyl-1*H*-pyrazole-1-sulfonamide

To a solution of *N*-dimethylsulfamoylpyrazole (188.0 g, 1.07 mol) in dry tetrahydrofuran (1500 mL) at -78 °C was added dropwise a solution of 2.5 M *n*-butyllithium (472 mL, 1.18 mol) in hexane while maintaining the temperature below -65 °C. Upon completion of the addition the reaction mixture was maintained at -78 °C for an additional 45 minutes, after which time a solution of hexachloroethane (279 g, 1.18 mol) in tetrahydrofuran (120 mL) was added dropwise. The reaction mixture was maintained for an hour at -78 °C, warmed to -20 °C and then quenched with water (1 L). The reaction mixture was extracted with methylene chloride (4x500 mL); the organic extracts were dried over magnesium sulfate and concentrated. The crude product was further purified by chromatography on silica gel using methylene chloride as eluent to afford the title product compound as a yellow oil (160 g).

^{1}H NMR ($CDCl_3$) δ 3.07 (d, 6H), 6.33 (s, 1H), 7.61 (s, 1H).

Step B: Preparation of 3-Chloropyrazole

To trifluoroacetic acid (290 mL) was added dropwise the chloropyrazole product (160 g) from Step A, and the reaction mixture was stirred at room temperature for 1.5 hours and then concentrated at reduced pressure. The residue was taken up in hexane, insoluble solids were filtered off, and the hexane was concentrated to afford the crude product as an oil. The crude product was further purified by chromatography on silica gel using ether/hexane (40:60) as eluent to afford the title product as a yellow oil (64.44 g).

^{1}H NMR ($CDCl_3$) δ 6.39 (s, 1H), 7.66 (s, 1H), 9.6 (br s, 1H).

Step C: Preparation of 3-Chloro-2-(3-chloro-1*H*-pyrazol-1-yl)pyridine

To a mixture of 2,3-dichloropyridine (92.60 g, 0.629 mol) and 3-chloropyrazole (i.e. the product of Step B) (64.44 g, 0.629 mol) in *N*,*N*-dimethylformamide (400 mL) was added potassium carbonate (147.78 g, 1.06 mol), and the reaction mixture was then heated to 100 °C for 36 hours. The reaction mixture was cooled to room temperature and slowly poured into ice water. The precipitated solids were filtered and washed with water. The solid filter cake was taken up in ethyl acetate, dried over magnesium sulfate and concentrated. The crude solid was chromatographed on silica gel using 20% ethyl acetate/hexane as eluent to afford the title product as a white solid (39.75 g).

^{1}H NMR ($CDCl_3$) δ 6.43 (s, 1H), 7.26 (m, 1H), 7.90 (d, 1H), 8.09 (s, 1H), 8.41 (d, 1H).

Step D: Preparation of 3-Chloro-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxylic acid

To a solution of the pyrazole product from Step C (39.75 g, 186 mmol) in dry tetrahydrofuran (400 mL) at -78 °C was added dropwise a solution of 2.0 M lithium diisopropylamide (93 mL, 186 mmol) in tetrahydrofuran. Carbon dioxide was bubbled through the amber solution for 14 minutes, after which time the solution became pale brownish-yellow. The reaction was made basic with 1N aqueous sodium hydroxide solution and extracted with ether (2x500 mL). The aqueous extracts were acidified with 6 N hydrochloric acid and extracted with ethyl acetate (3x500 mL). The ethyl acetate extracts were dried over magnesium sulfate and concentrated to afford the title product as an off-white solid (42.96 g). (Product from another run following similar procedure melted at 198-199 °C.)

^{1}H NMR (DMSO-d_6) δ 6.99 (s, 1H), 7.45 (m, 1H), 7.93 (d, 1H), 8.51 (d, 1H).

Step E: Preparation of 6-Chloro-2-[3-chloro-1-(3-chloro-2-pyridinyl)-1*H*-pyrazol-5-yl]-8-methyl-4*H*-3,1-benzoxazin-4-one

To a solution of methanesulfonyl chloride (6.96 g, 61.06 mmol) in acetonitrile (150 mL) was added dropwise a mixture of the carboxylic acid product from Step D (15.0 g, 58.16 mmol) and triethylamine (5.88 g, 58.16 mmol) in acetonitrile (150 mL) at -5 °C. The reaction mixture was then stirred for 30 minutes at 0 °C. Then, 2-amino-3-methyl-5-chlorobenzoic acid from Example 6, Step A (10.79 g, 58.16 mmol) was added, and stirring was continued for an additional 10 minutes. A solution of triethylamine (11.77 g, 116.5 mmol) in acetonitrile was then added dropwise while keeping the temperature below 10 °C. The reaction mixture was stirred 60 minutes at 0 °C, and then methanesulfonyl chloride (6.96 g, 61.06 mmol) was added. The reaction mixture was then warmed to room temperature and stirred for an additional 2 hours. The reaction mixture was then concentrated, and the crude product was chromatographed on silica gel using methylene chloride as eluent to afford the title product as a yellow solid (9.1 g).

^{1}H NMR ($CDCl_3$) δ 1.81 (s, 3H), 7.16 (s, 1H), 7.51 (m, 2H), 7.98 (d, 2H), 8.56 (d, 1H).

Step F: Preparation of 3-chloro-*N*-[4-chloro-2-methyl-6-[[(1-methylethyl)amino]-carbonyl]phenyl]-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxamide

To a solution of the benzoxazinone product of Step E (6.21 g, 15.21 mmol) in tetrahydrofuran (100 mL) was added isopropylamine (4.23 g, 72.74 mmol) and the reaction mixture was then heated to 60 °C, stirred for 1 hour and then cooled to room temperature. The tetrahydrofuran solvent was evaporated under reduced pressure, and the residual solid was purified by chromatography on silica gel to afford the title compound, a compound of the present invention, as a white solid (5.05 g) melting at 173-175 °C.

^{1}H NMR ($CDCl_3$) δ 1.23 (d, 6H), 2.18 (s, 3H), 4.21 (m, 1H), 5.97 (d, 1H), 7.01 (m, 1H), 7.20 (s, 1H), 7.24 (s, 1H), 7.41 (d, 1H), 7.83 (d, 1H), 8.43 (d, 1H), 10.15 (br s, 1H).

EXAMPLE 9

Preparation of 3-Chloro-*N*-[4-chloro-2-methyl-6-[(methylamino)carbonyl]phenyl]-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxamide

To a solution of the benzoxazinone product of Example 8, Step E (6.32 g, 15.47 mmol) in tetrahydrofuran (50 mL) was added methylamine (2.0 M solution in THF, 38 mL, 77.38 mmol), and the reaction mixture was heated to 60 °C, stirred for 1 hour and then cooled to room temperature. The tetrahydrofuran solvent was evaporated under reduced pressure, and the residual solid was purified by chromatography on silica gel to afford the title compound, a compound of the present invention, as a white solid (4.57 g) melting at 225-226 °C.

^{1}H NMR ($CDCl_3$) δ 2.15 (s, 3H), 2.93 (s, 3H), 6.21 (d, 1H), 7.06 (s, 1H), 7.18 (s, 1H), 7.20 (s, 1H), 7.42 (m, 1H), 7.83 (d, 1H), 8.42 (d, 1H), 10.08 (br s, 1H).

EXAMPLE 10

Preparation of 3-Bromo-*N*-[4-chloro-2-methyl-6-[[(1-methylethyl)amino]carbonyl]phenyl]-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxamide

Step A: Preparation of 3-Bromo-*N*,*N*-dimethyl-1*H*-pyrazole-1-sulfonamide

To a solution of *N*-dimethylsulfamoylpyrazole (44.0 g, 0.251 mol) in dry tetrahydrofuran (500 mL) at -78 °C was added dropwise a solution of *n*-butyllithium (2.5 M in hexane, 105.5 mL, 0.264 mol) while maintaining the temperature below -60 °C. A thick solid formed during the addition. Upon completion of the addition the reaction mixture was maintained for an additional 15 minutes, after which time a solution of 1,2-dibromo-tetrachloroethane (90 g, 0.276 mol) in tetrahydrofuran (150 mL) was added dropwise while maintaining the temperature below -70 °C. The reaction mixture turned a clear orange; stirring was continued for an additional 15 minutes. The -78 °C bath was removed and the reaction was quenched with water (600 mL). The reaction mixture was extracted with methylene chloride (4x), and the organic extracts were dried over magnesium sulfate and concentrated. The crude product was further purified by chromatography on silica gel using methylene chloride/hexane (50:50) as eluent to afford the title product as a clear colorless oil (57.04 g).

^{1}H NMR ($CDCl_3$) δ 3.07 (d, 6H), 6.44 (m, 1H), 7.62 (m, 1H).

Step B: Preparation of 3-Bromopyrazole

To trifluoroacetic acid (70 mL) was slowly added the bromopyrazole product (57.04 g) from Step A. The reaction mixture was stirred at room temperature for 30 minutes and then concentrated at reduced pressure. The residue was taken up in hexane, insoluble solids were

filtered off, and the hexane was evaporated to afford the crude product as an oil. The crude product was further purified by chromatography on silica gel using ethyl acetate/dichloromethane (10:90) as eluent to afford an oil. The oil was taken up in dichloromethane, neutralized with aqueous sodium bicarbonate solution, extracted with methylene chloride (3x), dried over magnesium sulfate and concentrated to afford the title product as a white solid (25.9 g), m.p. 61-64 °C.

^{1}H NMR ($CDCl_3$) δ 6.37 (d, 1H), 7.59 (d, 1H), 12.4 (br s, 1H).

Step C: Preparation of 2-(3-Bromo-1*H*-pyrazol-1-yl)-3-chloropyridine

To a mixture of 2,3-dichloropyridine (27.4 g, 185 mmol) and 3-bromopyrazole (i.e. the product of Step B) (25.4 g, 176 mmol) in dry *N*,*N*-dimethylformamide (88 mL) was added potassium carbonate (48.6 g, 352 mmol), and the reaction mixture was heated to 125 °C for 18 hours. The reaction mixture was cooled to room temperature and poured into ice water (800 mL). A precipitate formed. The precipitated solids were stirred for 1.5 hrs, filtered and washed with water (2x100 mL). The solid filter cake was taken up in methylene chloride and washed sequentially with water, 1N hydrochloric acid, saturated aqueous sodium bicarbonate solution, and brine. The organic extracts were then dried over magnesium sulfate and concentrated to afford 39.9 g of a pink solid. The crude solid was suspended in hexane and stirred vigorously for 1 hr. The solids were filtered, washed with hexane and dried to afford the title product as an off-white powder (30.4 g) determined to be > 94 % pure by NMR. This material was used without further purification in Step D.

^{1}H NMR ($CDCl_3$) δ 6.52 (s, 1H), 7.30 (dd, 1H), 7.92 (d, 1H), 8.05 (s, 1H), 8.43 (d, 1H).

Step D: Preparation of 3-Bromo-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxylic acid

To a solution of the pyrazole product from Step C (30.4 g, 118 mmol) in dry tetrahydrofuran (250 mL) at -76 °C was added dropwise a solution of lithium diisopropylamide (118 mmol) in tetrahydrofuran at such a rate as to maintain the temperature below -71 °C. The reaction mixture was stirred for 15 minutes at -76 °C, and carbon dioxide was then bubbled through for 10 minutes, causing warming to -57 °C. The reaction mixture was warmed to -20 °C and quenched with water. The reaction mixture was concentrated and then taken up in water (1 L) and ether (500 mL), and then aqueous sodium hydroxide solution (1 N, 20 mL) was added. The aqueous extracts were washed with ether and acidified with hydrochloric acid. The precipitated solids were filtered, washed with water and dried to afford the title product as a tan solid (27.7 g). (Product from another run following similar procedure melted at 200-201 °C.)

^{1}H NMR (DMSO-d_6) δ 7.25 (s, 1H), 7.68 (dd, 1H), 8.24 (d, 1H), 8.56 (d, 1H).

Step E: Preparation of 2-[3-Bromo-1-(3-chloro-2-pyridinyl)-1*H*-pyrazol-5-yl]-6-chloro-8-methyl-4*H*-3,1-benzoxazin-4-one

A procedure analogous to that of Example 6, Step D was used to convert the pyrazolecarboxylic acid product from Example 10, Step D (1.5 g, 4.96 mmol) and 2-amino-3-methyl-5-chlorobenzoic acid (0.92 g, 4.96 mmol) to the title product as a solid (1.21 g).
^{1}H NMR ($CDCl_3$) δ 2.01 (s, 3H), 7.29 (s, 1H), 7.42 (d, 1H), 7.95 (d, 1H), 8.04 (m, 1H), 8.25 (s, 1H), 8.26 (d, 1H).

Step F: Preparation of 3-Bromo-*N*-[4-chloro-2-methyl-6-[[(1-methylethyl)amino]-carbonyl]phenyl]-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxamide

To a solution of the benzoxazinone product of Step E (0.20 g, 0.44 mmol) in tetrahydrofuran was added isopropylamine (0.122 mL, 1.42 mmol), and the reaction mixture was heated to 60 °C for 90 minutes and then cooled to room temperature. The tetrahydrofuran solvent was evaporated under reduced pressure, and the residual solid was triturated with ether, filtered, and dried to afford the title compound, a compound of the present invention, as a solid (150 mg), m.p. 159-161 °C.
^{1}H NMR ($CDCl_3$) δ 1.22 (d, 6H), 2.19 (s, 3H), 4.21 (m, 1H), 5.99 (m, 1H), 7.05 (m, 1H), 7.22 (m, 2H), 7.39 (m, 1H), 7.82 (d, 1H), 8.41 (d, 1H).

EXAMPLE 11

Preparation of 3-Bromo-*N*-[4-chloro-2-methyl-6-[(methylamino)carbonyl]phenyl]-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxamide

To a solution of the benzoxazinone product of Example 10, Step E (0.20 g, 0.44 mmol) in tetrahydrofuran was added methylamine (2.0 M solution in THF, 0.514 mL, 1.02 mmol), and the reaction mixture was heated to 60 °C for 90 minutes and then cooled to room temperature. The tetrahydrofuran solvent was evaporated under reduced pressure, and the residual solid was triturated with ether, filtered, and dried to afford the title compound, a compound of the present invention, as a solid (40 mg), m.p. 162-164 °C.
^{1}H NMR ($CDCl_3$) δ 2.18 (s, 3H), 2.95 (s, 3H), 6.21 (m, 1H), 7.10 (s, 1H), 7.24 (m, 2H), 7.39 (m, 1H), 7.80 (d, 1H), 8.45 (d, 1H).

The following Example 12 illustrates an alternative preparation of 3-chloro-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxylic acid, which can be used to prepare, for example, 3-chloro-*N*-[4-chloro-2-methyl-6-[[(1-methylethyl)amino]carbonyl]phenyl]-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxamide and 3-chloro-*N*-[4-chloro-2-methyl-6-[(methylamino)carbonyl]phenyl]-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxamide, by further steps illustrated in Examples 8 and 9.

EXAMPLE 12

Preparation of 3-chloro-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxylic acid

Step A: Preparation of Ethyl 2-(3-chloro-2-pyridinyl)-5-oxo-3-pyrazolidinecarboxylate (alternatively named ethyl 1-(3-chloro-2-pyridinyl)-3-pyrazolidinone-5-carboxylate)

A 2-L four-necked flask equipped with a mechanical stirrer, thermometer, addition funnel, reflux condenser, and nitrogen inlet was charged with absolute ethanol (250 mL) and an ethanolic solution of sodium ethoxide (21%, 190 mL, 0.504 mol). The mixture was heated to reflux at about 83 °C. It was then treated with 3-chloro-2(1*H*)-pyridinone hydrazone (68.0 g, 0.474 mol). The mixture was re-heated to reflux over a period of 5 minutes. The yellow slurry was then treated dropwise with diethyl maleate (88.0 mL, 0.544 mol) over a period of 5 minutes. The reflux rate increased markedly during the addition. By the end of the addition all of the starting material had dissolved. The resulting orange-red solution was held at reflux for 10 minutes. After being cooled to 65 °C, the reaction mixture was treated with glacial acetic acid (50.0 mL, 0.873 mol). A precipitate formed. The mixture was diluted with water (650 mL), causing the precipitate to dissolve. The orange solution was cooled in an ice bath. Product began to precipitate at 28 °C. The slurry was held at about 2 °C for 2 hours. The product was isolated via filtration, washed with aqueous ethanol (40%, 3 x 50 mL), and then air-dried on the filter for about 1 hour. The title product compound was obtained as a highly crystalline, light orange powder (70.3 g, 55% yield). No significant impurities were observed by ^1H NMR.

^1H NMR (DMSO-d_6) δ 1.22 (t, 3H), 2.35 (d, 1H), 2.91 (dd, 1H), 4.20 (q, 2H), 4.84 (d, 1H), 7.20 (dd, 1H), 7.92 (d, 1H), 8.27 (d, 1H), 10.18 (s, 1H).

Step B: Preparation of Ethyl 3-chloro-1-(3-chloro-2-pyridinyl)-4,5-dihydro-1*H*-pyrazole-5-carboxylate (alternatively named ethyl 1-(3-chloro-2-pyridinyl)-3-chloro-2-pyrazoline-5-carboxylate)

To a 2-L four-necked flask equipped with a mechanical stirrer, thermometer, reflux condenser, and nitrogen inlet was charged acetonitrile (1000 mL), ethyl 2-(3-chloro-2-pyridinyl)-5-oxo-3-pyrazolidinecarboxylate (i.e. the product of Step A) (91.0 g, 0.337 mol) and phosphorus oxychloride (35.0 mL, 0.375 mol). Upon adding the phosphorus oxychloride, the mixture self-heated from 22 to 25 °C and a precipitate formed. The light-yellow slurry was heated to reflux at 83 °C over a period of 35 minutes, whereupon the precipitate dissolved. The resulting orange solution was held at reflux for 45 minutes, whereupon it had become black-green. The reflux condenser was replaced with a distillation head, and 650 mL of solvent was removed by distillation. A second 2-L four-necked flask equipped with a mechanical stirrer was charged with sodium bicarbonate (130 g, 1.55 mol) and water (400 mL). The concentrated reaction mixture was added to the sodium

bicarbonate slurry over a period of 15 minutes. The resulting, two-phase mixture was stirred vigorously for 20 minutes, at which time gas evolution had ceased. The mixture was diluted with dichloromethane (250 mL) and then was stirred for 50 minutes. The mixture was treated with Celite® 545 diatomaceous earth filter aid (11 g) and then filtered to remove a black, tarry substance that inhibited phase separation. Since the filtrate was slow to separate into distinct phases, it was diluted with dichloromethane (200 mL) and water (200 mL) and treated with more Celite® 545 (15 g). The mixture was filtered, and the filtrate was transferred to a separatory funnel. The heavier, deep green organic layer was separated. A rag layer (50 mL) was refiltered and then added to the organic layer. The organic solution (800 mL) was treated with magnesium sulfate (30 g) and silica gel (12 g), and the slurry was stirred magnetically for 30 minutes. The slurry was filtered to remove the magnesium sulfate and silica gel, which had become deep blue-green. The filter cake was washed with dichloromethane (100 mL). The filtrate was concentrated on a rotary evaporator. The product consisted of dark amber oil (92.0 g, 93% yield). The only appreciable impurities observed by ^{1}H NMR were 1% starting material and 0.7% acetonitrile.

^{1}H NMR (DMSO-d_6) δ 1.15 (t, 3H), 3.26 (dd, 1H), 3.58 (dd, 1H), 4.11 (q, 2H), 5.25 (dd, 1H), 7.00 (dd, 1H), 7.84 (d, 1H), 8.12 (d, 1H).

Step C: Preparation of Ethyl 3-chloro-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxylate (alternatively named ethyl 1-(3-chloro-2-pyridinyl)-3-chloropyrazole-5-carboxylate)

A 2-L four-necked flask equipped with a mechanical stirrer, thermometer, reflux condenser, and nitrogen inlet was charged with ethyl 3-chloro-1-(3-chloro-2-pyridinyl)-4,5-dihydro-1*H*-pyrazole-5-carboxylate (i.e. the product of Step B) (95% pure, 99.5 g, 0.328 mol), acetonitrile (1000 mL) and sulfuric acid (98%, 35.0 mL, 0.661 mol). The mixture self-heated from 22 to 35 °C upon adding the sulfuric acid. After being stirred for several minutes, the mixture was treated with potassium persulfate (140 g, 0.518 mol). The slurry was heated to reflux at 84 °C for 4.5 hours. The resulting orange slurry while still warm (50–65 °C) was filtered to remove a fine, white precipitate. The filter cake was washed with acetonitrile (50 mL). The filtrate was concentrated to about 500 mL on a rotary evaporator. A second 2-L four-necked flask equipped with a mechanical stirrer was charged with water (1250 mL). The concentrated reaction mass was added to the water over a period of about 5 minutes. The product was isolated via filtration, washed with aqueous acetonitrile (25%, 3 x 125 mL), washed once with water (100 mL), and then dried overnight *in vacuo* at room temperature. The product consisted of a crystalline, orange powder (79.3 g, 82% yield). The only appreciable impurities observed by ^{1}H NMR were about 1.9% water and 0.6% acetonitrile.

^{1}H NMR (DMSO-d_6) δ 1.09 (t, 3H), 4.16 (q, 2H), 7.31 (s, 1H), 7.71 (dd, 1H), 8.38 (d, 1H), 8.59 (d, 1H).

Step D: Preparation of 3-Chloro-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxylic acid (alternatively named 1-(3-chloro-2-pyridinyl)-3-chloropyrazole-5-carboxylic acid)

A 1-L four-necked flask equipped with a mechanical stirrer, thermometer, and nitrogen inlet was charged with ethyl 3-chloro-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxylate (i.e. the product of Step C) (97.5% pure, 79.3 g, 0.270 mol), methanol (260 mL), water (140 mL) and sodium hydroxide pellets (13.0 g, 0.325 mol). Upon adding the sodium hydroxide the mixture self-heated from 22 to 35 °C, and the starting material began to dissolve. After being stirred for 45 minutes under ambient conditions, all of the starting material had dissolved. The resulting deep orange-brown solution was concentrated to about 250 mL on a rotary evaporator. The concentrated reaction mixture was then diluted with water (400 mL). The aqueous solution was extracted with ether (200 mL). Then the aqueous layer was transferred to a 1-L Erlenmeyer flask equipped with a magnetic stirrer. The solution was treated dropwise with concentrated hydrochloric acid (36.0 g, 0.355 mol) over a period of about 10 minutes. The product was isolated via filtration, reslurried with water (2 x 200 mL), cover washed once with water (100 mL) and then air-dried on the filter for 1.5 hours. The product consisted of a crystalline, light brown powder (58.1 g, 83% yield). About 0.7% ether was the only appreciable impurity observed by ^{1}H NMR.

^{1}H NMR (DMSO-d_6) δ 7.20 (s, 1H), 7.68 (dd, 1H), 8.25 (d, 1H), 8.56 (d, 1H), 13.95 (br s, 1H).

The following Example 13 illustrates an alternative preparation of 3-bromo-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxylic acid, which can be used to prepare, for example, 3-bromo-*N*-[4-chloro-2-methyl-6-[[(1-methylethyl)amino]carbonyl]phenyl]-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxamide and 3-bromo-*N*-[4-chloro-2-methyl-6-[(methylamino)carbonyl]phenyl]-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxamide, by further steps illustrated in Examples 10 and 11.

EXAMPLE 13

Preparation of 3-Bromo-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxylic acid

Step A1: Preparation of Ethyl 3-bromo-1-(3-chloro-2-pyridinyl)-4,5-dihydro-1*H*-pyrazole-5-carboxylate (alternatively named ethyl 1-(3-chloro-2-pyridinyl)-3-bromo-2-pyrazoline-5-carboxylate) using phosphorus oxybromide

A 1-L four-necked flask equipped with a mechanical stirrer, thermometer, reflux condenser, and nitrogen inlet was charged with acetonitrile (400 mL), ethyl 2-(3-chloro-2-pyridinyl)-5-oxo-3-pyrazolidinecarboxylate (i.e. the product of Example 12, Step A) (50.0 g, 0.185 mol) and phosphorus oxybromide (34.0 g, 0.119 mol). The orange slurry was heated to reflux at 83 °C over a period of 20 minutes. The resulting turbid, orange solution was

held at reflux for 75 minutes, at which time a dense, tan, crystalline precipitate had formed. The reflux condenser was replaced with a distillation head, and a cloudy, colorless distillate (300 mL) was collected. A second 1-L four-necked flask equipped with a mechanical stirrer was charged with sodium bicarbonate (45 g, 0.54 mol) and water (200 mL). The concentrated reaction mixture was added to the sodium bicarbonate slurry over a period of 5 minutes. The resulting two-phase mixture was stirred vigorously for 5 minutes, at which time gas evolution had ceased. The mixture was diluted with dichloromethane (200 mL) and then was stirred for 75 minutes. The mixture was treated with 5 g of Celite® 545 diatomaceous filter aid and then filtered to remove a brown, tarry substance. The filtrate was transferred to a separatory funnel. The brown organic layer (400 mL) was separated and then was treated with magnesium sulfate (15 g) and Darco® G60 activated charcoal (2.0 g). The resulting slurry was stirred magnetically for 15 minutes and then filtered to remove the magnesium sulfate and charcoal. The green filtrate was treated with silica gel (3 g) and stirred for several minutes. The deep blue-green silica gel was removed by filtration, and the filtrate was concentrated on a rotary evaporator. The product consisted of a light amber oil (58.6 g, 95% yield), which crystallized upon standing. The only appreciable impurity observed by ^{1}H NMR was 0.3% acetonitrile.

^{1}H NMR (DMSO-d_6) δ 1.15 (t, 3H), 3.29 (dd, 1H), 3.60 (dd, 1H), 4.11 (q, 2H), 5.20 (dd, 1H), 6.99 (dd, 1H), 7.84 (d, 1H), 8.12 (d, 1H).

Step A2: Preparation of Ethyl 3-bromo-1-(3-chloro-2-pyridinyl)-4,5-dihydro-1*H*-pyrazole-5-carboxylate using phosphorus pentabromide

A 1-L four-necked flask equipped with a mechanical stirrer, thermometer, reflux condenser, and nitrogen inlet was charged with acetonitrile (330 mL), ethyl 2-(3-chloro-2-pyridinyl)-5-oxo-3-pyrazolidinecarboxylate (i.e. the product of Example 12, Step A) (52.0 g, 0.193 mol), and phosphorus pentabromide (41.0 g, 0.0952 mol). The orange slurry was heated to reflux at 84 °C over a period of 20 minutes. The resulting brick-red mixture was held at reflux for 90 minutes, at which time a dense tan crystalline precipitate had formed. The reflux condenser was replaced with a distillation head, and a cloudy, colorless distillate (220 mL) was collected. A second 1-L four-necked flask equipped with a mechanical stirrer was charged with sodium bicarbonate (40 g, 0.48 mol) and water (200 mL). The concentrated reaction mixture was added to the sodium bicarbonate slurry over a period of 5 minutes. The resulting, two-phase mixture was stirred vigorously for 10 minutes, at which time gas evolution had ceased. The mixture was diluted with dichloromethane (200 mL) and then was stirred for 10 minutes. The mixture was treated with Celite® 545 diatomaceous filter aid (5 g) and then filtered to remove a purple, tarry substance. The filter cake was washed with dichloromethane (50 mL). The filtrate was transferred to a separatory funnel. The purple-red organic layer (400 mL) was separated and then was treated with magnesium sulfate (15 g) and Darco® G60 activated charcoal (2.2 g). The slurry was stirred

magnetically for 40 minutes. The slurry was filtered to remove the magnesium sulfate and charcoal. The filtrate was concentrated on a rotary evaporator. The product consisted of a dark amber oil (61.2 g, 95% yield), which crystallized upon standing. The only appreciable impurity observed by ^{1}H NMR was 0.7% acetonitrile.

^{1}H NMR (DMSO-d_6) δ 1.15 (t, 3H), 3.29 (dd, 1H), 3.60 (dd, 1H), 4.11 (q, 2H), 5.20 (dd, 1H), 6.99 (dd, 1H), 7.84 (d, 1H), 8.12 (d, 1H).

Step B: Preparation of Ethyl 3-bromo-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxylate (alternatively named ethyl 1-(3-chloro-2-pyridinyl)-3-bromopyrazole-5-carboxylate)

A 1-L four-necked flask equipped with a mechanical stirrer, thermometer, reflux condenser, and nitrogen inlet was charged with ethyl 3-bromo-1-(3-chloro-2-pyridinyl)-4,5-dihydro-1*H*-pyrazole-5-carboxylate (i.e. the product of Steps A1 and A2) (40.2 g, 0.121 mol), acetonitrile (300 mL) and sulfuric acid (98%, 13.0 mL, 0.245 mol). The mixture self-heated from 22 to 36 °C upon adding the sulfuric acid. After being stirred for several minutes, the mixture was treated with potassium persulfate (48.0 g, 0.178 mol). The slurry was heated to reflux at 84 °C for 2 hours. The resulting orange slurry while still warm (50–65 °C) was filtered to remove a white precipitate. The filter cake was washed with acetonitrile (2 x 50 mL). The filtrate was concentrated to about 200 mL on a rotary evaporator. A second 1-L four-necked flask equipped with a mechanical stirrer was charged with water (400 mL). The concentrated reaction mass was added to the water over a period of about 5 minutes. The product was isolated via filtration, washed sequentially with aqueous acetonitrile (20%, 100 mL) and water (75 mL), and was then air-dried on the filter for 1 hour. The product consisted of a crystalline, orange powder (36.6 g, 90% yield). The only appreciable impurities observed by ^{1}H NMR were about 1% of an unknown and 0.5% acetonitrile.

^{1}H NMR (DMSO-d_6) δ 1.09 (t, 3H), 4.16 (q, 2H), 7.35 (s, 1H), 7.72 (dd, 1H), 8.39 (d, 1H), 8.59 (d, 1H).

Step C: Preparation of 3-Bromo-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxylic acid (alternatively named 1-(3-chloro-2-pyridinyl)-3-bromopyrazole-5-carboxylic acid)

A 300-mL four-necked flask equipped with a mechanical stirrer, thermometer, and nitrogen inlet was charged with ethyl 3-bromo-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxylate (i.e. the product of Step B) (98.5% pure, 25.0 g, 0.0756 mol), methanol (75 mL), water (50 mL), and sodium hydroxide pellets (3.30 g, 0.0825 mol). Upon adding the sodium hydroxide the mixture self-heated from 29 to 34 °C and the starting material began to dissolve. After being stirred for 90 minutes under ambient conditions, all of the starting material had dissolved. The resulting dark orange solution was concentrated to

about 90 mL on a rotary evaporator. The concentrated reaction mixture was then diluted with water (160 mL). The aqueous solution was extracted with ether (100 mL). Then the aqueous layer was transferred to a 500-mL Erlenmeyer flask equipped with a magnetic stirrer. The solution was treated dropwise with concentrated hydrochloric acid (8.50 g, 0.0839 mol) over a period of about 10 minutes. The product was isolated via filtration, reslurried with water (2 x 40 mL), cover washed once with water (25 mL), and then air-dried on the filter for 2 hours. The product consisted of a crystalline, tan powder (20.9 g, 91% yield). The only appreciable impurities observed by ^{1}H NMR were about 0.8% of an unknown and 0.7% ether.

^{1}H NMR (DMSO-d_6) δ 7.25 (s, 1H), 13.95 (br s, 1H), 8.56 (d, 1H), 8.25 (d, 1H), 7.68 (dd, 1H).

The following Example 14 illustrates an alternative preparation of ethyl 3-bromo-1-(3-chloro-2-pyridinyl)-4,5-dihydro-1*H*-pyrazole-5-carboxylate, which can be used to prepare, for example, ethyl 3-bromo-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxylate (i.e. product of Example 13, Step B).

EXAMPLE 14

Preparation of Ethyl 3-bromo-1-(3-chloro-2-pyridinyl)-4,5-dihydro-1*H*-pyrazole-5-carboxylate from ethyl 3-chloro-1-(3-chloro-2-pyridinyl)-4,5-dihydro-1*H*-pyrazole-5-carboxylate using hydrogen bromide

Hydrogen bromide was passed through a solution of ethyl 3-chloro-1-(3-chloro-2-pyridinyl)-4,5-dihydro-1*H*-pyrazole-5-carboxylate (i.e. product of Example 12, Step B) (8.45 g, 29.3 mmol) in dibromomethane (85 mL). After 90 minutes the gas flow was terminated, and the reaction mixture was washed with aqueous sodium bicarbonate solution (100 mL). The organic phase was dried and evaporated under reduced pressure to give the title product as an oil (9.7 g, 99% yield), which crystallized on standing.

^{1}H NMR ($CDCl_3$) δ 1.19 (t, 3H), 3.24 (1/2 of AB in ABX pattern, J = 9.3, 17.3 Hz, 1H), 3.44 (1/2 of AB in ABX pattern, J = 11.7, 17.3 Hz, 1H), 4.18 (q, 2H), 5.25 (X of ABX, 1H, J = 9.3, 11.9 Hz), 6.85 (dd, J = 4.7, 7.7 Hz, 1H), 7.65 (dd, J = 1.6, 7.8 Hz, 1H), 8.07 (dd, J = 1.6, 4.8 Hz, 1H).

The following Example 15 illustrates the preparation of ethyl 1-(3-chloro-2-pyridinyl)-4,5-dihydro-3-[[(4-methylphenyl)sulfonyl]oxy]-1*H*-pyrazole-5-carboxylate, which can be used to prepare ethyl 3-bromo-1-(3-chloro-2-pyridinyl)-4,5-dihydro-1*H*-pyrazole-5-carboxylate by procedures similar to that described in Example 14.

EXAMPLE 15

Preparation of ethyl 1-(3-chloro-2-pyridinyl)-4,5-dihydro-3-[[(4-methylphenyl)sulfonyl]oxy]-1*H*-pyrazole-5-carboxylate

Triethylamine (3.75 g, 37.1 mmol) was added dropwise to a mixture of ethyl 2-(3-chloro-2-pyridinyl)-5-oxo-3-pyrazolidinecarboxylate (i.e. the product of Example 12, Step A) (10.0 g, 37.1 mmol) and *p*-toluenesulfonyl chloride (7.07 g, 37.1 mmol) in dichloromethane (100 mL) at 0 °C. Further portions of *p*-toluenesulfonyl chloride (0.35 g, 1.83 mmol) and triethylamine (0.19 g, 1.88 mmol) were added. The reaction mixture was then allowed to warm to room temperature and was stirred overnight. The mixture was then diluted with dichloromethane (200 mL) and washed with water (3 x 70 mL). The organic phase was dried and evaporated to leave the title product as an oil (13.7 g, 87% yield), which slowly formed crystals. Product recrystallized from ethyl acetate/hexanes melted at 99.5–100 °C.

IR (nujol) ν 1740, 1638, 1576, 1446, 1343, 1296, 1228, 1191, 1178, 1084, 1027, 948, 969, 868, 845 cm^{-1}.

^{1}H NMR ($CDCl_3$) δ 1.19 (t, 3H), 2.45 (s, 3H), 3.12 (1/2 of AB in ABX pattern, J = 17.3, 9 Hz, 1H), 3.33 (1/2 of AB in ABX pattern, J = 17.5, 11.8 Hz, 1H), 4.16 (q, 2H), 5.72 (X of ABX, J = 9, 11.8 Hz, 1H), 6.79 (dd, J = 4.6, 7.7 Hz, 1H), 7.36 (d, J = 8.4 Hz, 2H), 7.56 (dd, J = 1.6, 7.8 Hz, 1H), 7.95 (d, J = 8.4 Hz, 2H), 8.01 (dd, J = 1.4, 4.6 Hz, 1H).

EXAMPLE 16

Preparation of *N*-[4-Chloro-2-methyl-6-[(methylamino)carbonyl]phenyl]-1-(3-chloro-2-pyridinyl)-3-(2,2,2-trifluoroethoxy)-1*H*-pyrazole-5-carboxamide

Step A: Preparation of Ethyl 1-(3-chloro-2-pyridinyl)-2,3-dihydro-3-oxo-1*H*-pyrazole-5-carboxylate

To a suspension of ethyl 2-(3-chloro-2-pyridinyl)-5-oxo-3-pyrazolidinecarboxylate (i.e. product of Example 12, Step A) (27 g, 100 mmol) stirred in dry acetonitrile (200 mL) was added sulfuric acid (20 g, 200 mmol) in one portion. The reaction mixture thinned to form a pale green, nearly clear solution before thickening again to form a pale yellow suspension. Potassium persulfate (33 g, 120 mmol) was added in one portion, and then the reaction mixture was heated at gentle reflux for 3.5 hours. After cooling using an ice bath, a precipitate of white solid was removed by filtration and discarded. The filtrate was diluted with water (400 mL) and then extracted three times with ethyl ether (700 mL total). Concentration of the combined ether extracts to a reduced volume (75 mL) caused precipitation of an off-white solid (3.75 g), which was collected by filtration. The ether mother liquor was further concentrated to yield a second crop of an off-white precipitate (4.2 g), which was also collected by filtration. An off-white solid also precipitated from the

aqueous phase; this solid (4.5 g) was collected by filtration to provide a combined total of 12.45 g of the title compound.

^{1}H NMR (DMSO-d_6) δ 1.06 (t, 3H), 4.11 (q, 2H), 6.34 (s, 1H), 7.6 (t, 1H), 8.19 (d, 1H), 8.5 (d, 1H), 10.6 (s, 1H).

Step B: Preparation of Ethyl 1-(3-chloro-2-pyridinyl)-3-(2,2,2-trifluoroethoxy)-1*H*-pyrazole-5-carboxylate

To a suspension of ethyl 1-(3-chloro-2-pyridinyl)-2,3-dihydro-3-oxo-1*H*-pyrazole-5-carboxylate (i.e. product of Step A) (0.8 g, 3 mmol) stirred in dry acetonitrile (15 mL) at –5 °C was added potassium carbonate (0.85 g, 6.15 mmol). The suspension was stirred for 15 minutes at 20 °C. The stirred suspension was then cooled to 5 °C, and 2,2,2-trifluoroethyl trifluoromethanesulfonate (0.8 g, 3.45 mmol) was added dropwise. The reaction mixture was warmed to room temperature and then heated to reflux, at which time thin layer chromatography showed the reaction to be complete. Water (25 mL) was added to the reaction mixture, which was then extracted with ethyl ether. The ether extract was dried over magnesium sulfate and concentrated to yield the title product compound (1.05 g) as a pale yellow oil.

^{1}H NMR ($CDCl_3$) δ 1.21 (t, 3H), 4.20 (q, 2H), 4.63 (q, 2H), 6.53 (s, 1H), 7.4 (t, 1H), 7.9 (d, 1H), 8.5 (d, 1H).

Step C: Preparation of 1-(3-Chloro-2-pyridinyl)-3-(2,2,2-trifluoroethoxy)-1*H*-pyrazole-5-carboxylic acid

To a stirred solution of ethyl 1-(3-chloro-2-pyridinyl)-3-(2,2,2-trifluoroethoxy)-1*H*-pyrazole-5-carboxylate (i.e. product of Step B) (0.92 g, 2.8 mmol) in methanol (15 mL) was added water (5 mL), which caused the reaction mixture to become cloudy. An aqueous solution of sodium hydroxide (50%, 1.5 g, 19.2 mmol) was added dropwise, and the reaction mixture was stirred at room temperature for 30 minutes, during which time the reaction mixture became again clear. Water (20 mL) was added and the reaction mixture was extracted with ethyl ether, which was discarded. The aqueous phase was acidified to pH 2 using concentrated hydrochloric acid and then extracted with ethyl acetate (50 mL). The ethyl acetate extract, which was washed with water (20 mL) and brine (20 mL), dried over magnesium sulfate and concentrated to give the title compound, isolated as a white solid (0.8 g).

^{1}H NMR (DMSO-d_6) δ 4.9 (q, 2H), 6.75 (s, 1H), 7.6 (t, 1H), 8.2 (d, 1H), 8.55 (d, 1H), 13.7 (bs, 1H).

Step D: Preparation of 6-Chloro-8-methyl-2*H*-3,1-benzoxazine-2,4(1*H*)-dione

To a suspension of 2-amino-3-methyl-5-chlorobenzoic acid (i.e. product of Example 6, Step A) (97 g, 520 mmol) stirred in dry dioxane (750 mL) at room temperature, trichloromethyl chloroformate (63 g, 320 mmol) was added dropwise. The reaction mixture

exothermically warmed slowly to 42 °C, and the solid almost completely dissolved before a thick suspension formed again. After the suspension was stirred at ambient temperature for 2.5 hours, the title compound was isolated by filtration, washed with ethyl ether, and dried to yield the title product compound, obtained as a white solid (98 g).

^{1}H NMR (DMSO-d_6) δ 2.3 (s, 3H), 7.70 (s, 1H), 7.75 (s, 1H), 11.2 (s, 1H).

Step E: Preparation of 6-Chloro-2-[1-(3-chloro-2-pyridinyl)-3-(2,2,2-trifluoroethoxy)-1*H*-pyrazol-5-yl]-8-methyl-4*H*-3,1-benzoxazin-4-one

To a suspension of 1-(3-chloro-2-pyridinyl)-3-(2,2,2-trifluoroethoxy)-1*H*-pyrazole-5-carboxylic acid (i.e. product of Step C) (7.9 g, 24 mmol) stirred in dichloromethane (100 mL) was added *N,N*-dimethylformamide (4 drops). Oxalyl chloride (4.45 g, 35 mmol) was added dropwise over a period of 45 minutes. The resulting solution was stirred at room temperature for 4 hours and then concentrated under vacuum. The isolated acid chloride was dissolved in dry acetonitrile (10 mL) and added to a suspension of 6-chloro-8-methyl-2*H*-3,1-benzoxazine-2,4(1*H*)-dione (i.e. product of Step D) (4.9 g, 23 mmol) stirred in dry acetonitrile (14 mL). Pyridine (10 mL) was added, and the solution heated at reflux 6 hours. After cooling using an ice bath, a precipitate of white solid (9.15 g) was collected. The ^{1}H NMR spectrum of the collected precipitate showed peaks consistent with the title compound and residual 6-chloro-8-methyl-2*H*-3,1-benzoxazine-2,4(1*H*)-dione starting material. A small portion of the collected precipitate was recrystallized from acetonitrile to yield the pure title product melting at 178–180 °C.

^{1}H NMR (DMSO-d_6) δ 1.72 (s, 3H), 4.96 (q, 2H), 7.04 (s, 1H), 7.7 (t, 1H), 7.75 (s, 1H), 7.9 (s, 1H), 8.3 (d, 1H), 8.6 (d, 1H).

Step F: Preparation of *N*-[4-chloro-2-methyl-6-[(methylamino)carbonyl]phenyl]-1-(3-chloro-2-pyridinyl)-3-(2,2,2-trifluoroethoxy)-1*H*-pyrazole-5-carboxamide

To a suspension of the 6-chloro-2-[1-(3-chloro-2-pyridinyl)-3-(2,2,2-trifluoroethoxy)-1*H*-pyrazol-5-yl]-8-methyl-4*H*-3,1-benzoxazin-4-one (i.e. precipitate product of Step E) (3.53 g, 7.5 mmol) in tetrahydrofuran (15 mL), methylamine (2.0 M solution in THF, 11 mL, 22 mmol) was added dropwise, and the resulting solution was stirred at room temperature for 45 minutes. Thin layer chromatography then showed the reaction to be complete. Ethyl ether (100 mL) was added, and the reaction mixture was stirred for 2 hours while a precipitate formed. The precipitate was collected by filtration and then recrystallized from acetonitrile to yield a white solid (0.82 g). A second crop of white solid (0.35 g) precipitated from the acetonitrile mother liquor and was collected by filtration. The initial ether/tetrahydrofuran mother liquor was concentrated to dryness, and the residual solid was recrystallized from acetonitrile to yield a third crop of white solid (0.95 g). The three crops

were combined, totaling 2.12 g (after drying) of the title compound, a compound of the present invention, isolated as a white solid, melting at 195-197 °C.

^{1}H NMR ($CDCl_3$) δ 2.18 (s, 3H), 2.92 (d, 3H), 4.66 (q, 2H), 6.15 (q, 1H), 6.6 (s, 1H), 7.2 (s, 1H), 7.25 (s, 1H), 7.35 (t, 1H), 7.8 (d, 1H), 8.45 (d, 1H), 10.0 (s, 1H).

The following Example 17 illustrates an alternative preparation of 1-(3-chloro-2-pyridinyl)-3-(trifluoromethyl)-1*H*-pyrazole-5-carboxylic acid, which can be used to prepare, for example, 1-(3-chloro-2-pyridinyl)-*N*-[2-methyl-6-[[(1-methylethyl)amino]carbonyl]-phenyl]-3-(trifluoromethyl)-1*H*-pyrazole-5-carboxamide, by further steps illustrated in Examples 4.

EXAMPLE 17

Preparation of 1-(3-chloro-2-pyridinyl)-3-(trifluoromethyl)-1*H*-pyrazole-5-carboxylic acid

Step A: Preparation of 3-chloro-2(1*H*)-pyridinone (2,2,2-trifluoro-1-methylethylidene)hydrazone

1,1,1-Trifluoroacetone (7.80 g, 69.6 mmol) was added to 3-chloro-2(1*H*)-pyridinone hydrazone (alternatively named (3-chloro-pyridin-2-yl)-hydrazine) (10 g, 69.7 mmol) at 20–25 °C. After the addition was complete, the mixture was stirred for about 10 minutes. The solvent was removed under reduced pressure and the mixture partitioned between ethyl acetate (100 mL) and saturated aqueous sodium carbonate solution (100 mL). The organic layer was dried and evaporated. Chromatography on silica gel (eluted with ethyl acetate) gave the product as an off-white solid (11 g, 66% yield), m.p. 64–64.5 °C (after crystallization from ethyl acetate/hexanes).

IR (nujol) ν 1629, 1590, 1518, 1403, 1365, 1309, 1240, 1196, 1158, 1100, 1032, 992, 800 cm^{-1}.

^{1}H NMR ($CDCl_3$) δ 2.12 (s, 3H), 6.91–6.86 (m, 1H), 7.64–7.61 (m, 1H), 8.33–8.32 (m, 2H).

MS *m/z* 237 (M^+).

Step B: Preparation of ethyl hydrogen ethanedioate (3-chloro-2-pyridinyl)(2,2,2-trifluoro-1-methylethylidene)hydrazide (alternatively named ethyl hydrogen ethanedioate (3-chloro-2-pyridinyl)(2,2,2-trifluoro-1-methylethylidene)hydrazine)

Triethylamine (20.81 g, 0.206 mol) was added to 3-chloro-2(1*H*)-pyridinone (2,2,2-trifluoro-1-methylethylidene)hydrazone (i.e. the product of Step A) (32.63 g, 0.137 mol) in dichloromethane (68 mL) at 0 °C. Ethyl chlorooxoacetate (18.75 g, 0.137 mol) in dichloromethane (69 mL) was added dropwise to the mixture at 0 °C. The mixture was allowed to warm to 25 °C over about 2 hours. The mixture was cooled to 0 °C and a further portion of ethyl chlorooxoacetate (3.75 g, 27.47 mmol) in dichloromethane (14 mL) was added dropwise. After about an additional 1 hour, the mixture was diluted with dichloromethane (about 450 mL), and the mixture was washed with water (2 x 150 mL).

The organic layer was dried and evaporated. Chromatography on silica gel (eluted with 1:1 ethyl acetate–hexanes) gave the product as a solid (42.06 g, 90% yield), m.p. 73.0–73.5 °C (after crystallization from ethyl acetate/hexanes).

IR (nujol) ν 1751, 1720, 1664, 1572, 1417, 1361, 1330, 1202, 1214, 1184, 1137, 1110, 1004, 1043, 1013, 942, 807, 836 cm^{-1}.

^{1}H NMR (DMSO-d_6, 115 °C) 1.19 (t, 3H), 1.72 (br s, 3H), 4.25 (q, 2H), 7.65 (dd, J = 8.3, 4.7 Hz, 1H), 8.20 (dd, J = 7.6, 1.5 Hz, 1H), 8.55 (d, J = 3.6 Hz, 1H).

MS m/z 337 (M^+).

Step C: Preparation of ethyl 1-(3-chloro-2-pyridinyl)-4,5-dihydro-5-hydroxy-3-(trifluoromethyl)-1*H*-pyrazole-5-carboxylate

Ethyl hydrogen ethanedioate (3-chloro-2-pyridinyl)(2,2,2-trifluoro-1-methylethylidene)hydrazide (i.e. the product of Step B) (5 g, 14.8 mmol) in dimethyl sulfoxide (25mL) was added to tetrabutylammonium fluoride hydrate (10 g) in dimethyl sulfoxide (25 mL) over 8 hours. When the addition was complete, the mixture was poured into acetic acid (3.25 g) in water (25 mL). After stirring at 25 °C overnight, the mixture was then extracted with toluene (4 x 25 mL), and the combined toluene extracts were washed with water (50 mL), dried and evaporated to give a solid. Chromatography on silica gel (eluted with 1:2 ethyl acetate–hexanes) gave the product as a solid (2.91 g, 50% yield, containing about 5% of 3-chloro-2(1*H*)-pyridinone (2,2,2-trifluoro-1-methylethylidene)hydrazone), m.p. 78–78.5 °C (after recrystallization from ethyl acetate/hexanes).

IR (nujol) ν 3403, 1726, 1618, 1582, 1407, 1320, 1293, 1260, 1217, 1187, 1150, 1122, 1100, 1067, 1013, 873, 829 cm^{-1}.

^{1}H NMR ($CDCl_3$) δ 1.19 (s, 3H), 3.20 (1/2 of ABZ pattern, J = 18 Hz, 1H), 3.42 (1/2 of ABZ pattern, J = 18 Hz, 1H), 4.24 (q, 2H), 6.94 (dd, J = 7.9, 4.9 Hz, 1H), 7.74 (dd, J = 7.7, 1.5 Hz, 1H), 8.03 (dd, J = 4.7, 1.5 Hz, 1H).

MS m/z 319 (M^+).

Step D: Preparation of ethyl 1-(3-chloro-2-pyridinyl)-3-(trifluoromethyl)-1*H*-pyrazole-5-carboxylate

Sulfuric acid (concentrated, 2 drops) was added to ethyl 1-(3-chloro-2-pyridinyl)-4,5-dihydro-5-hydroxy-3-(trifluoromethyl)-1*H*-pyrazole-5-carboxylate (i.e. the product of Step C) (1 g, 2.96 mmol) in acetic acid (10 mL) and the mixture was warmed to 65 °C for about 1 hour. The mixture was allowed to cool to 25 °C and most of the acetic acid was removed under reduced pressure. The mixture was partitioned between saturated aqueous sodium carbonate solution (100 mL) and ethyl acetate (100 mL). The aqueous layer was further extracted with ethyl acetate (100 mL). The combined organic extracts were dried and evaporated to give the product as an oil (0.66 g, 77% yield).

IR (neat) ν 3147, 2986, 1734, 1577, 1547, 1466, 1420, 1367, 1277, 1236, 1135, 1082, 1031, 973, 842, 802 cm^{-1}.

^1H NMR ($CDCl_3$) δ 1.23 (t, 3H), 4.25 (q, 2H), 7.21 (s, 1H), 7.48 (dd, J = 8.1, 4.7 Hz, 1H), 7.94 (dd, J = 6.6, 2 Hz, 1H), 8.53 (dd, J = 4.7, 1.5 Hz, 1H).

MS m/z 319 (M^+).

Step E: Preparation of 1-(3-chloro-2-pyridinyl)-3-(trifluoromethyl)-1*H*-pyrazole-5-carboxylic acid

Potassium hydroxide (0.5 g, 85%, 2.28 mmol) in water (1 mL) was added to ethyl 1-(3-chloro-2-pyridinyl)-3-(trifluoromethyl)-1*H*-pyrazole-5-carboxylate (i.e. the product of Step D) (0.66 g, 2.07 mmol) in ethanol (3 mL). After about 30 minutes, the solvent was removed under reduced pressure, and the mixture was dissolved in water (40 mL). The solution was washed with ethyl acetate (20 mL). The aqueous layer was acidified with concentrated hydrochloric acid and was extracted with ethyl acetate (3 x 20 mL). The combined extracts were dried and evaporated to give the product as a solid (0.53 g, 93% yield), m.p. 178–179 °C (after crystallization from hexanes–ethyl acetate).

IR (nujol) ν 1711, 1586, 1565, 1550, 1440, 1425, 1292, 1247, 1219, 1170, 1135, 1087, 1059, 1031, 972, 843, 816 cm^{-1}.

^1H NMR (DMSO-d_6) δ 7.61 (s, 1H), 7.77 (m, 1H), 8.30 (d, 1H), 8.60 (s, 1H).

Examples 18 and 19 illustrate alternatives to reaction conditions described in Example 10, Step E and Example 8, Step E, respectively.

EXAMPLE 18

Preparation of 2-[3-bromo-1-(3-chloro-2-pyridinyl)-1*H*-pyrazol-5-yl]-6-chloro-8-methyl-4*H*-3,1-benzoxazin-4-one

Methanesulfonyl chloride (1.0 mL, 1.5 g, 13 mmol) was dissolved in acetonitrile (10 mL), and the mixture was cooled to –5 °C. A solution of 3-bromo-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxylic acid (i.e. the pyrazolecarboxylic acid product of Example 10, Step D) (3.02 g, 10 mmol) and pyridine (1.4 mL, 1.4 g, 17 mmol) in acetonitrile (10 mL) was added dropwise over 5 minutes at –5 to 0 °C. A slurry formed during the addition. The mixture was stirred 5 minutes at this temperature, and then a mixture of 2-amino-3-methyl-5-chlorobenzoic acid (i.e. the product of Example 6 Step A) (1.86 g, 10 mmol) and pyridine (2.8 mL, 2.7 g, 35 mmol) in acetonitrile (10 mL) was added, rinsing with more acetonitrile (5 mL). The mixture was stirred 15 minutes at –5 to 0 °C, and then methanesulfonyl chloride (1.0 mL, 1.5 mL, 13 mmol) in acetonitrile (5 mL) was added dropwise over 5 minutes at a temperature of –5 to 0 °C. The reaction mixture was stirred 15 minutes more at this temperature, then allowed to warm slowly to room temperature, and stirred 4 h. Water (20 mL) was added dropwise, and the mixture was stirred 15 minutes. Then the mixture was filtered, and the solids were washed with 2:1 acetonitrile–water (3 × 3

mL), then with acetonitrile (2 × 3 mL), and dried under nitrogen to afford the title product as a light yellow powder, 4.07 g (90.2% crude yield), melting at 203–205 °C. HPLC of the product using a Zorbax® RX-C8 chromatography column (4.6 mm × 25 cm, eluent 25–95% acetonitrile/ pH 3 water) showed a major peak corresponding to the title compound and having 95.7% of total chromatogram peak area.

^{1}H NMR (DMSO-d_6) δ 1.72 (s, 3H) 7.52 (s, 1H), 7.72–7.78 (m, 2H), 7.88 (m, 1H), 8.37 (dd, 1H), 8.62 (dd, 1H).

EXAMPLE 19

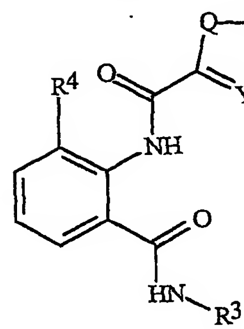
Preparation of 6-chloro-2-[3-chloro-1-(3-chloro-2-pyridinyl)-1*H*-pyrazol-5-yl]-8-methyl-4*H*-3,1-benzoxazin-4-one

Methanesulfonyl chloride (1.0 mL, 1.5 g, 13 mmol) was dissolved in acetonitrile (10 mL), and the mixture was cooled to –5 °C. A solution of 3-chloro-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxylic acid (i.e. the carboxylic acid product of Example 8, Step D) (2.58 g, 10 mmol) and pyridine (1.4 mL, 1.4 g, 17 mmol) in acetonitrile (10 mL) was added dropwise over 5 minutes at –5 to 0 °C. A slurry formed during the addition. The mixture was stirred 5 minutes at this temperature, and then 2-amino-3-methyl-5-chlorobenzoic acid (i.e. the product from Example 6, Step A) (1.86 g, 10 mmol) was added all at once. Then a solution of pyridine (2.8 mL, 2.7 g, 35 mmol) in acetonitrile (10 mL) was added dropwise in 5 min at –5 to 0 °C. The mixture was stirred 15 minutes at –5 to 0 °C, and then methanesulfonyl chloride (1.0 mL, 1.5 mL, 13 mmol) in acetonitrile (5 mL) was added dropwise in 5 min at –5 to 0 °C. The reaction mixture was stirred 15 minutes at this temperature, then allowed to warm slowly to room temperature, and stirred 4 h. Water (15 mL) was added dropwise, and the mixture was stirred 15 minutes. Then the mixture was filtered, and the solids were washed with 2:1 acetonitrile–water (3 × 3 mL), then with acetonitrile (2 × 3 mL), and dried under nitrogen to afford the title product as a pale yellow powder, 3.83 g (94.0% crude yield), melting at 199–201 °C. HPLC of the product using a Zorbax® RX-C8 chromatography column (4.6 mm × 25 cm, eluent 25–95% acetonitrile/ pH 3 water) showed a major peak corresponding to the title compound and having 97.8% of total chromatogram peak area.

^{1}H NMR (DMSO-d_6) δ 1.72 (s, 3H), 7.48 (s, 1H), 7.74–7.80 (m, 2H), 7.87 (m, 1H), 8.37 (dd, 1H), 8.62 (dd, 1H).

By the procedures described herein together with methods known in the art, the following compounds of Table 1 can be prepared. The following abbreviations are used in the Tables which follow: *t* means tertiary, *s* means secondary, *n* means normal, *i* means iso, Me means methyl, Et means ethyl, Pr means propyl, *i*-Pr means isopropyl, and Bu means butyl.

TABLE 1



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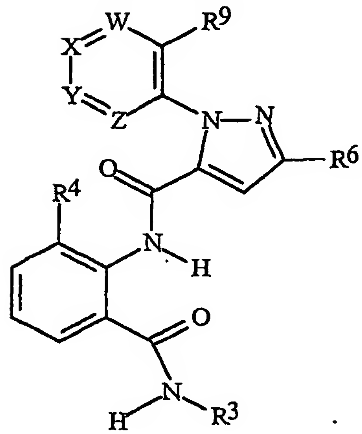
i-Pr	Cl	NMe	N	CH	CCF_3	*i*-Pr	Cl	NMe	N	CH	CC_2F_5
i-Pr	Br	NMe	N	CH	CCF_3	*i*-Pr	Br	NMe	N	CH	CC_2F_5
i-Pr	I	NMe	N	CH	CCF_3	*i*-Pr	I	NMe	N	CH	CC_2F_5
i-Pr	F	NMe	N	CH	CCF_3	*i*-Pr	F	NMe	N	CH	CC_2F_5
i-Pr	H	NMe	N	CH	CCF_3	*i*-Pr	H	NMe	N	CH	CC_2F_5
i-Pr	Et	NMe	N	CH	CCF_3	*i*-Pr	Et	NMe	N	CH	CC_2F_5
i-Pr	Me	NEt	N	CH	CCF_3	*t*-Bu	Me	NMe	N	CH	CCF_3
i-Pr	Cl	NEt	N	CH	CCF_3	*t*-Bu	Cl	NMe	N	CH	CCF_3
i-Pr	Br	NEt	N	CH	CCF_3	*t*-Bu	Br	NMe	N	CH	CCF_3
i-Pr	I	NEt	N	CH	CCF_3	*t*-Bu	I	NMe	N	CH	CCF_3
i-Pr	F	NEt	N	CH	CCF_3	*t*-Bu	F	NMe	N	CH	CCF_3
i-Pr	H	NEt	N	CH	CCF_3	*t*-Bu	H	NMe	N	CH	CCF_3
i-Pr	Et	NEt	N	CH	CCF_3	*t*-Bu	Et	NMe	N	CH	CCF_3

TABLE 2



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CH	CH	CH	CH	*i*-Pr	Cl	CF_3	Me
CH	CH	CH	CH	*t*-Bu	Cl	CF_3	Me
CH	CH	CH	CH	*i*-Pr	Br	CF_3	Me
CH	CH	CH	CH	*t*-Bu	Br	CF_3	Me
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CH	CH	CH	CH	*i*-Pr	Me	CN	Me
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CH	CH	CH	CH	*t*-Bu	Cl	CN	Me
CH	CH	CH	CH	*i*-Pr	Br	CN	Me
CH	CH	CH	CH	*t*-Bu	Br	CN	Me
CH	CH	CH	CH	*i*-Pr	Me	CF_3	F

W	X	Y	Z	R^3	R^4	R^6	R^9
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CH	CH	CH	CH	*t*-Bu	Br	CF_3	F
CH	CH	CH	CH	*i*-Pr	Me	Cl	F
CH	CH	CH	CH	*t*-Bu	Me	Cl	F
CH	CH	CH	CH	*i*-Pr	Cl	Cl	F
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CH	CH	CH	CH	*i*-Pr	Cl	CF_3	CN

W	X	Y	Z	R^3	R^4	R^6	R^9
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CH	CH	CH	N	*t*-Bu	Cl	CN	F
CH	CH	CH	N	*i*-Pr	Br	CN	F
CH	CH	CH	N	*t*-Bu	Br	CN	F
CH	CH	CH	N	*i*-Pr	Me	CF_3	Cl
CH	CH	CH	N	*t*-Bu	Me	CF_3	Cl
CH	CH	CH	N	*i*-Pr	Cl	CF_3	Cl
CH	CH	CH	N	*t*-Bu	Cl	CF_3	Cl
CH	CH	CH	N	*i*-Pr	Br	CF_3	Cl

W	X	Y	Z	R^3	R^4	R^6	R^9
CH	CH	CH	N	*t*-Bu	Br	CF_3	Cl
CH	CH	CH	N	*i*-Pr	Me	Cl	Cl
CH	CH	CH	N	*t*-Bu	Me	Cl	Cl
CH	CH	CH	N	*i*-Pr	Cl	Cl	Cl
CH	CH	CH	N	*t*-Bu	Cl	Cl	Cl
CH	CH	CH	N	*i*-Pr	Br	Cl	Cl
CH	CH	CH	N	*t*-Bu	Br	Cl	Cl
CH	CH	CH	N	*i*-Pr	Me	Br	Cl
CH	CH	CH	N	*t*-Bu	Me	Br	Cl
CH	CH	CH	N	*i*-Pr	Cl	Br	Cl
CH	CH	CH	N	*t*-Bu	Cl	Br	Cl
CH	CH	CH	N	*i*-Pr	Br	Br	Cl
CH	CH	CH	N	*t*-Bu	Br	Br	Cl
CH	CH	CH	N	*i*-Pr	Me	CN	Cl
CH	CH	CH	N	*t*-Bu	Me	CN	Cl
CH	CH	CH	N	*i*-Pr	Cl	CN	Cl
CH	CH	CH	N	*t*-Bu	Cl	CN	Cl
CH	CH	CH	N	*i*-Pr	Br	CN	Cl
CH	CH	CH	N	*t*-Bu	Br	CN	Cl
CH	CH	CH	N	*i*-Pr	Me	CF_3	Br
CH	CH	CH	N	*t*-Bu	Me	CF_3	Br
CH	CH	CH	N	*i*-Pr	Cl	CF_3	Br
CH	CH	CH	N	*t*-Bu	Cl	CF_3	Br
CH	CH	CH	N	*i*-Pr	Br	CF_3	Br
CH	CH	CH	N	*t*-Bu	Br	CF_3	Br
CH	CH	CH	N	*i*-Pr	Me	Cl	Br
CH	CH	CH	N	*t*-Bu	Me	Cl	Br
CH	CH	CH	N	*i*-Pr	Cl	Cl	Br
CH	CH	CH	N	*t*-Bu	Cl	Cl	Br
CH	CH	CH	N	*i*-Pr	Br	Cl	Br
CH	CH	CH	N	*t*-Bu	Br	Cl	Br
CH	CH	CH	N	*i*-Pr	Me	Br	Br
CH	CH	CH	N	*t*-Bu	Me	Br	Br
CH	CH	CH	N	*i*-Pr	Cl	Br	Br
CH	CH	CH	N	*t*-Bu	Cl	Br	Br
CH	CH	CH	N	*i*-Pr	Br	Br	Br
CH	CH	CH	N	*t*-Bu	Br	Br	Br

W	X	Y	Z	R^3	R^4	R^6	R^9
CH	CH	CH	N	*i*-Pr	Me	CN	Br
CH	CH	CH	N	*t*-Bu	Me	CN	Br
CH	CH	CH	N	*i*-Pr	Cl	CN	Br
CH	CH	CH	N	*t*-Bu	Cl	CN	Br
CH	CH	CH	N	*i*-Pr	Br	CN	Br
CH	CH	CH	N	*t*-Bu	Br	CN	Br
CH	CH	CH	N	*i*-Pr	Me	CF_3	CN
CH	CH	CH	N	*t*-Bu	Me	CF_3	CN
CH	CH	CH	N	*i*-Pr	Cl	CF_3	CN
CH	CH	CH	N	*t*-Bu	Cl	CF_3	CN
CH	CH	CH	N	*i*-Pr	Br	CF_3	CN
CH	CH	CH	N	*t*-Bu	Br	CF_3	CN
CH	CH	CH	N	*i*-Pr	Me	Cl	CN
CH	CH	CH	N	*t*-Bu	Me	Cl	CN
CH	CH	CH	N	*i*-Pr	Cl	Cl	CN
CH	CH	CH	N	*t*-Bu	Cl	Cl	CN
CH	CH	CH	N	*i*-Pr	Br	Cl	CN
CH	CH	CH	N	*t*-Bu	Br	Cl	CN
CH	CH	CH	N	*i*-Pr	Me	Br	CN
CH	CH	CH	N	*t*-Bu	Me	Br	CN
CH	CH	CH	N	*i*-Pr	Cl	Br	CN
CH	CH	CH	N	*t*-Bu	Cl	Br	CN
CH	CH	CH	N	*i*-Pr	Br	Br	CN
CH	CH	CH	N	*t*-Bu	Br	Br	CN
CH	CH	CH	N	*i*-Pr	Me	CN	CN
CH	CH	CH	N	*t*-Bu	Me	CN	CN
CH	CH	CH	N	*i*-Pr	Cl	CN	CN
CH	CH	CH	N	*t*-Bu	Cl	CN	CN
CH	CH	CH	N	*i*-Pr	Br	CN	CN
CH	CH	CH	N	*t*-Bu	Br	CN	CN
CH	CH	CH	CH	Me	Me	CF_3	F
CH	CH	CH	CH	Et	Me	CF_3	F
CH	CH	CH	CH	$CH(CH_3)CH_2OCH_3$	Me	CF_3	F
CH	CH	CH	CH	$CH(CH_3)CH_2SCH_3$	Me	CF_3	F
CH	CH	CH	CH	propargyl	Me	CF_3	F
CH	CH	CH	CH	Me	Me	CF_3	Cl
CH	CH	CH	CH	Et	Me	CF_3	Cl

W	X	Y	Z	R^3	R^4	R^6	R^9
CH	CH	CH	CH	$CH(CH_3)CH_2OCH_3$	Me	CF_3	Cl
CH	CH	CH	CH	$CH(CH_3)CH_2SCH_3$	Me	CF_3	Cl
CH	CH	CH	CH	propargyl	Me	CF_3	Cl
CH	CH	CH	CH	Me	Me	Br	F
CH	CH	CH	CH	Et	Me	Br	F
CH	CH	CH	CH	$CH(CH_3)CH_2OCH_3$	Me	Br	F
CH	CH	CH	CH	$CH(CH_3)CH_2SCH_3$	Me	Br	F
CH	CH	CH	CH	propargyl	Me	Br	F
CH	CH	CH	CH	Me	Me	Br	Cl
CH	CH	CH	CH	Et	Me	Br	Cl
CH	CH	CH	CH	$CH(CH_3)CH_2OCH_3$	Me	Br	Cl
CH	CH	CH	CH	$CH(CH_3)CH_2SCH_3$	Me	Br	Cl
CH	CH	CH	CH	propargyl	Me	Br	Cl
CH	CH	CH	CH	Me	Cl	CF_3	F
CH	CH	CH	CH	Et	Cl	CF_3	F
CH	CH	CH	CH	$CH(CH_3)CH_2OCH_3$	Cl	CF_3	F
CH	CH	CH	CH	$CH(CH_3)CH_2SCH_3$	Cl	CF_3	F
CH	CH	CH	CH	propargyl	Cl	CF_3	F
CH	CH	CH	CH	Me	Cl	CF_3	Cl
CH	CH	CH	CH	Et	Cl	CF_3	Cl
CH	CH	CH	CH	$CH(CH_3)CH_2OCH_3$	Cl	CF_3	Cl
CH	CH	CH	CH	$CH(CH_3)CH_2SCH_3$	Cl	CF_3	Cl
CH	CH	CH	CH	propargyl	Cl	CF_3	Cl
CH	CH	CH	CH	Me	Cl	Br	F
CH	CH	CH	CH	Et	Cl	Br	F
CH	CH	CH	CH	$CH(CH_3)CH_2OCH_3$	Cl	Br	F
CH	CH	CH	CH	$CH(CH_3)CH_2SCH_3$	Cl	Br	F
CH	CH	CH	CH	propargyl	Cl	Br	F
CH	CH	CH	CH	Me	Cl	Br	Cl
CH	CH	CH	CH	Et	Cl	Br	Cl
CH	CH	CH	CH	$CH(CH_3)CH_2OCH_3$	Cl	Br	Cl
CH	CH	CH	CH	$CH(CH_3)CH_2SCH_3$	Cl	Br	Cl
CH	CH	CH	CH	propargyl	Cl	Br	Cl
CH	CH	CH	N	Me	Me	CF_3	F
CH	CH	CH	N	Et	Me	CF_3	F
CH	CH	CH	N	$CH(CH_3)CH_2OCH_3$	Me	CF_3	F
CH	CH	CH	N	$CH(CH_3)CH_2SCH_3$	Me	CF_3	F

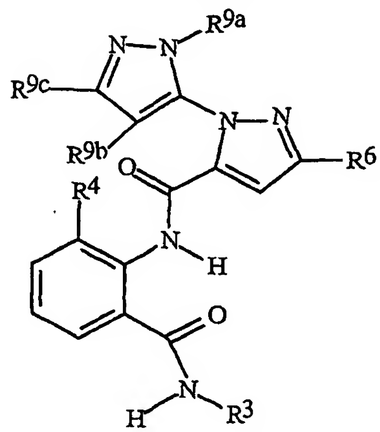
W	X	Y	Z	R^3	R^4	R^6	R^9
CH	CH	CH	N	propargyl	Me	CF_3	F
CH	CH	CH	N	Me	Me	CF_3	Cl
CH	CH	CH	N	Et	Me	CF_3	Cl
CH	CH	CH	N	$CH(CH_3)CH_2OCH_3$	Me	CF_3	Cl
CH	CH	CH	N	$CH(CH_3)CH_2SCH_3$	Me	CF_3	Cl
CH	CH	CH	N	propargyl	Me	CF_3	Cl
CH	CH	CH	N	Me	Me	Br	F
CH	CH	CH	N	Et	Me	Br	F
CH	CH	CH	N	$CH(CH_3)CH_2OCH_3$	Me	Br	F
CH	CH	CH	N	$CH(CH_3)CH_2SCH_3$	Me	Br	F
CH	CH	CH	N	propargyl	Me	Br	F
CH	CH	CH	N	Me	Me	Br	Cl
CH	CH	CH	N	Et	Me	Br	Cl
CH	CH	CH	N	$CH(CH_3)CH_2OCH_3$	Me	Br	Cl
CH	CH	CH	N	$CH(CH_3)CH_2SCH_3$	Me	Br	Cl
CH	CH	CH	N	propargyl	Me	Br	Cl
CH	CH	CH	N	Me	Cl	CF_3	F
CH	CH	CH	N	Et	Cl	CF_3	F
CH	CH	CH	N	$CH(CH_3)CH_2OCH_3$	Cl	CF_3	F
CH	CH	CH	N	$CH(CH_3)CH_2SCH_3$	Cl	CF_3	F
CH	CH	CH	N	propargyl	Cl	CF_3	F
CH	CH	CH	N	Me	Cl	CF_3	Cl
CH	CH	CH	N	Et	Cl	CF_3	Cl
CH	CH	CH	N	$CH(CH_3)CH_2OCH_3$	Cl	CF_3	Cl
CH	CH	CH	N	$CH(CH_3)CH_2SCH_3$	Cl	CF_3	Cl
CH	CH	CH	N	propargyl	Cl	CF_3	Cl
CH	CH	CH	N	Me	Cl	Br	F
CH	CH	CH	N	Et	Cl	Br	F
CH	CH	CH	N	$CH(CH_3)CH_2OCH_3$	Cl	Br	F
CH	CH	CH	N	$CH(CH_3)CH_2SCH_3$	Cl	Br	F
CH	CH	CH	N	propargyl	Cl	Br	F
CH	CH	CH	N	Me	Cl	Br	Cl
CH	CH	CH	N	Et	Cl	Br	Cl
CH	CH	CH	N	$CH(CH_3)CH_2OCH_3$	Cl	Br	Cl
CH	CH	CH	N	$CH(CH_3)CH_2SCH_3$	Cl	Br	Cl
CH	CH	CH	N	propargyl	Cl	Br	Cl
C-Cl	CH	CH	CH	*i*-Pr	Me	CF_3	Cl

W	X	Y	Z	R^3	R^4	R^6	R^9
C-F	CH	CH	CH	*i*-Pr	Me	CF_3	F
CH	CH	CH	CH	*i*-Pr	Me	CF_3	ethynyl
CH	CH	CH	CH	*i*-Pr	Me	CF_3	I
CH	CH	CH	CH	*i*-Pr	Me	CF_3	SO_2Me
C-Cl	CH	CH	CH	*i*-Pr	Cl	CF_3	Cl
C-F	CH	CH	CH	*i*-Pr	Cl	CF_3	F
CH	CH	CH	CH	*i*-Pr	Cl	CF_3	ethynyl
CH	CH	CH	CH	*i*-Pr	Cl	CF_3	I
CH	CH	CH	CH	*i*-Pr	Cl	CF_3	SO_2Me
C-Cl	CH	CH	CH	*i*-Pr	Me	Br	Cl
C-F	CH	CH	CH	*i*-Pr	Me	Br	F
CH	CH	CH	CH	*i*-Pr	Me	Br	ethynyl
CH	CH	CH	CH	*i*-Pr	Me	Br	I
CH	CH	CH	CH	*i*-Pr	Me	Br	SO_2Me
C-Cl	CH	CH	CH	*i*-Pr	Cl	Br	Cl
C-F	CH	CH	CH	*i*-Pr	Cl	Br	F
CH	CH	CH	CH	*i*-Pr	Cl	Br	ethynyl
CH	CH	CH	CH	*i*-Pr	Cl	Br	I
CH	CH	CH	CH	*i*-Pr	Cl	Br	SO_2Me
C-Cl	CH	CH	N	*i*-Pr	Me	CF_3	Cl
C-F	CH	CH	N	*i*-Pr	Me	CF_3	F
CH	CH	CH	N	*i*-Pr	Me	CF_3	ethynyl
CH	CH	CH	N	*i*-Pr	Me	CF_3	I
CH	CH	CH	N	*i*-Pr	Me	CF_3	SO_2Me
C-Cl	CH	CH	N	*i*-Pr	Cl	CF_3	Cl
C-F	CH	CH	N	*i*-Pr	Cl	CF_3	F
CH	CH	CH	N	*i*-Pr	Cl	CF_3	ethynyl
CH	CH	CH	N	*i*-Pr	Cl	CF_3	I
CH	CH	CH	N	*i*-Pr	Cl	CF_3	SO_2Me
C-Cl	CH	CH	N	*i*-Pr	Me	Br	Cl
C-F	CH	CH	N	*i*-Pr	Me	Br	F
CH	CH	CH	N	*i*-Pr	Me	Br	ethynyl
CH	CH	CH	N	*i*-Pr	Me	Br	I
CH	CH	CH	N	*i*-Pr	Me	Br	SO_2Me
C-Cl	CH	CH	N	*i*-Pr	Cl	Br	Cl
C-F	CH	CH	N	*i*-Pr	Cl	Br	F
CH	CH	CH	N	*i*-Pr	Cl	Br	ethynyl

W	X	Y	Z	R^3	R^4	R^6	R^9
CH	CH	CH	N	*i*-Pr	Cl	Br	I
CH	CH	CH	N	*i*-Pr	Cl	Br	SO_2Me
CH	N	CH	N	*i*-Pr	Me	CF_3	H
CH	N	CH	N	*i*-Pr	Me	CF_3	Me
CH	N	CH	N	*i*-Pr	Me	CF_3	Cl
CH	N	CH	N	*i*-Pr	Cl	CF_3	H
CH	N	CH	N	*i*-Pr	Cl	CF_3	Me
CH	N	CH	N	*i*-Pr	Cl	CF_3	Cl
CH	N	CH	N	*i*-Pr	Me	CN	H
CH	N	CH	N	*i*-Pr	Me	CN	Me
CH	N	CH	N	*i*-Pr	Me	CN	Cl
CH	N	CH	N	*i*-Pr	Cl	CN	H
CH	N	CH	N	*i*-Pr	Cl	CN	Me
CH	N	CH	N	*i*-Pr	Cl	CN	Cl
CH	N	CH	N	*i*-Pr	Me	Br	H
CH	N	CH	N	*i*-Pr	Me	Br	Me
CH	N	CH	N	*i*-Pr	Me	Br	Cl
CH	N	CH	N	*i*-Pr	Cl	Br	H
CH	N	CH	N	*i*-Pr	Cl	Br	Me
CH	N	CH	N	*i*-Pr	Cl	Br	Cl
CH	N	CH	N	*t*-Bu	Me	CF_3	H
CH	N	CH	N	*t*-Bu	Me	CF_3	Me
CH	N	CH	N	*t*-Bu	Me	CF_3	Cl
CH	N	CH	N	*t*-Bu	Cl	CF_3	H
CH	N	CH	N	*t*-Bu	Cl	CF_3	Me
CH	N	CH	N	*t*-Bu	Cl	CF_3	Cl
CH	N	CH	N	*t*-Bu	Me	CN	H
CH	N	CH	N	*t*-Bu	Me	CN	Me
CH	N	CH	N	*t*-Bu	Me	CN	Cl
CH	N	CH	N	*t*-Bu	Cl	CN	H
CH	N	CH	N	*t*-Bu	Cl	CN	Me
CH	N	CH	N	*t*-Bu	Cl	CN	Cl
CH	N	CH	N	*t*-Bu	Me	Br	H
CH	N	CH	N	*t*-Bu	Me	Br	Me
CH	N	CH	N	*t*-Bu	Me	Br	Cl
CH	N	CH	N	*t*-Bu	Cl	Br	H
CH	N	CH	N	*t*-Bu	Cl	Br	Me

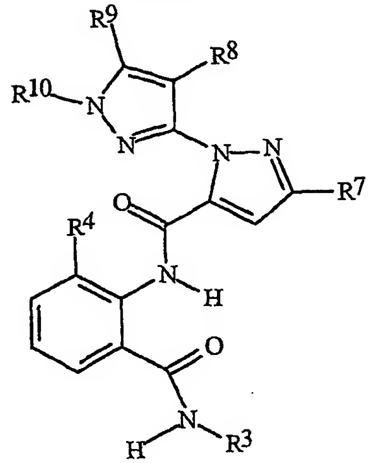
W	X	Y	Z	R^3	R^4	R^6	R^9
CH	N	CH	N	*t*-Bu	Cl	Br	Cl
CH	CH	N	N	*i*-Pr	Me	CF_3	H
CH	CH	N	N	*i*-Pr	Me	CF_3	Me
CH	CH	N	N	*i*-Pr	Me	CF_3	Cl
CH	CH	N	N	*i*-Pr	Cl	CF_3	H
CH	CH	N	N	*i*-Pr	Cl	CF_3	Me
CH	CH	N	N	*i*-Pr	Cl	CF_3	Cl
CH	CH	N	N	*i*-Pr	Me	CN	H
CH	CH	N	N	*i*-Pr	Me	CN	Me
CH	CH	N	N	*i*-Pr	Me	CN	Cl
CH	CH	N	N	*i*-Pr	Cl	CN	H
CH	CH	N	N	*i*-Pr	Cl	CN	Me
CH	CH	N	N	*i*-Pr	Cl	CN	Cl
CH	CH	N	N	*i*-Pr	Me	Br	H
CH	CH	N	N	*i*-Pr	Me	Br	Me
CH	CH	N	N	*i*-Pr	Me	Br	Cl
CH	CH	N	N	*i*-Pr	Cl	Br	H
CH	CH	N	N	*i*-Pr	Cl	Br	Me
CH	CH	N	N	*i*-Pr	Cl	Br	Cl
CH	CH	N	N	*i*-Pr	Me	CF_3	H
CH	CH	N	N	*i*-Pr	Me	CF_3	Me
CH	CH	N	N	*i*-Pr	Me	CF_3	Cl
CH	CH	N	N	*i*-Pr	Cl	CF_3	H
CH	CH	N	N	*i*-Pr	Cl	CF_3	Me
CH	CH	N	N	*i*-Pr	Cl	CF_3	Cl
CH	CH	N	N	*i*-Pr	Me	CN	H
CH	CH	N	N	*i*-Pr	Me	CN	Me
CH	CH	N	N	*i*-Pr	Me	CN	Cl
CH	CH	N	N	*i*-Pr	Cl	CN	H
CH	CH	N	N	*i*-Pr	Cl	CN	Me
CH	CH	N	N	*i*-Pr	Cl	CN	Cl
CH	CH	N	N	*i*-Pr	Me	Br	H
CH	CH	N	N	*i*-Pr	Me	Br	Me
CH	CH	N	N	*i*-Pr	Me	Br	Cl
CH	CH	N	N	*i*-Pr	Cl	Br	H
CH	CH	N	N	*i*-Pr	Cl	Br	Me
CH	CH	N	N	*i*-Pr	Cl	Br	Cl

TABLE 3



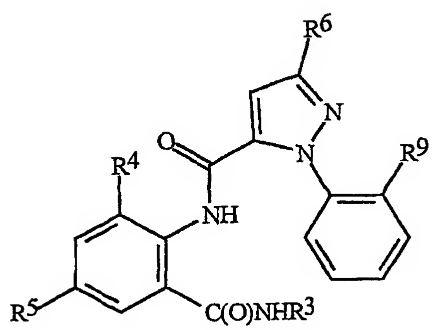
R^4	R^6	R^3	R^{9a}	R^{9b}	R^{9c}	R^4	R^6	R^3	R^{9a}	R^{9b}	R^{9c}
Me	CF_3	*i*-Pr	Me	H	H	Me	CF_3	*t*-Bu	Me	H	H
Me	CF_3	*i*-Pr	Me	H	Me	Me	CF_3	*t*-Bu	Me	H	Me
Me	CF_3	*i*-Pr	Me	Cl	H	Me	CF_3	*t*-Bu	Me	Cl	H
Me	CF_3	*i*-Pr	Me	Cl	Me	Me	CF_3	*t*-Bu	Me	Cl	Me
Me	CF_3	*i*-Pr	Me	Me	Me	Me	CF_3	*t*-Bu	Me	Me	Me
Cl	CF_3	*i*-Pr	Me	H	H	Cl	CF_3	*t*-Bu	Me	H	H
Cl	CF_3	*i*-Pr	Me	H	Me	Cl	CF_3	*t*-Bu	Me	H	Me
Cl	CF_3	*i*-Pr	Me	Cl	H	Cl	CF_3	*t*-Bu	Me	Cl	H
Cl	CF_3	*i*-Pr	Me	Cl	Me	Cl	CF_3	*t*-Bu	Me	Cl	Me
Cl	CF_3	*i*-Pr	Me	Me	Me	Cl	CF_3	*t*-Bu	Me	Me	Me

TABLE 4



R^4	R^6	R^3	R^{9a}	R^{9b}	R^{9c}	R^4	R^6	R^3	R^{9a}	R^{9b}	R^{9c}
Me	CF_3	*i*-Pr	Me	H	Me	Me	CF_3	*t*-Bu	Me	H	Me
Me	CF_3	*i*-Pr	Me	Me	Me	Me	CF_3	*t*-Bu	Me	Me	Me
Me	CF_3	*i*-Pr	Cl	H	Me	Me	CF_3	*t*-Bu	Cl	H	Me
Me	CF_3	*i*-Pr	Cl	Me	Me	Me	CF_3	*t*-Bu	Cl	Me	Me
Cl	CF_3	*i*-Pr	Me	H	Me	Cl	CF_3	*t*-Bu	Me	H	Me
Cl	CF_3	*i*-Pr	Me	Me	Me	Cl	CF_3	*t*-Bu	Me	Me	Me
Cl	CF_3	*i*-Pr	Cl	H	Me	Cl	CF_3	*t*-Bu	Cl	H	Me
Cl	CF_3	*i*-Pr	Cl	Me	Me	Cl	CF_3	*t*-Bu	Cl	Me	Me

TABLE 5



R^4	R^5	R^6	R^3	R^9	R^4	R^5	R^6	R^3	R^9
CH_3	F	CF_3	Me	Cl	Cl	Br	Cl	Me	Br
CH_3	F	CF_3	Et	Cl	Cl	Br	Cl	Et	Br
CH_3	F	CF_3	*i*-Pr	Cl	Cl	Br	Cl	*i*-Pr	Br
CH_3	F	CF_3	*t*-Bu	Cl	Cl	Br	Cl	*t*-Bu	Br
CH_3	F	CF_3	Me	Br	Cl	Br	Br	Me	Cl

R^4	R^5	R^6	R^3	R^9	R^4	R^5	R^6	R^3	R^9
CH_3	F	CF_3	Et	Br	Cl	Br	Br	Et	Cl
CH_3	F	CF_3	*i*-Pr	Br	Cl	Br	Br	*i*-Pr	Cl
CH_3	F	CF_3	*t*-Bu	Br	Cl	Br	Br	*t*-Bu	Cl
CH_3	F	Cl	Me	Cl	Cl	Br	Br	Me	Br
CH_3	F	Cl	Et	Cl	Cl	Br	Br	Et	Br
CH_3	F	Cl	*i*-Pr	Cl	Cl	Br	Br	*i*-Pr	Br
CH_3	F	Cl	*t*-Bu	Cl	Cl	Br	Br	*t*-Bu	Br
CH_3	F	Cl	Me	Br	Cl	I	CF_3	Me	Cl
CH_3	F	Cl	Et	Br	Cl	I	CF_3	Et	Cl
CH_3	F	Cl	*i*-Pr	Br	Cl	I	CF_3	*i*-Pr	Cl
CH_3	F	Cl	*t*-Bu	Br	Cl	I	CF_3	*t*-Bu	Cl
CH_3	F	Br	Me	Cl	Cl	I	CF_3	Me	Br
CH_3	F	Br	Et	Cl	Cl	I	CF_3	Et	Br
CH_3	F	Br	*i*-Pr	Cl	Cl	I	CF_3	*i*-Pr	Br
CH_3	F	Br	*t*-Bu	Cl	Cl	I	CF_3	*t*-Bu	Br
CH_3	F	Br	Me	Br	Cl	I	Cl	Me	Cl
CH_3	F	Br	Et	Br	Cl	I	Cl	Et	Cl
CH_3	F	Br	*i*-Pr	Br	Cl	I	Cl	*i*-Pr	Cl
CH_3	F	Br	*t*-Bu	Br	Cl	I	Cl	*t*-Bu	Cl
CH_3	Cl	CF_3	Me	Cl	Cl	I	Cl	Me	Br
CH_3	Cl	CF_3	Et	Cl	Cl	I	Cl	Et	Br
CH_3	Cl	CF_3	*i*-Pr	Cl	Cl	I	Cl	*i*-Pr	Br
CH_3	Cl	CF_3	*t*-Bu	Cl	Cl	I	Cl	*t*-Bu	Br
CH_3	Cl	CF_3	Me	Br	Cl	I	Br	Me	Cl
CH_3	Cl	CF_3	Et	Br	Cl	I	Br	Et	Cl
CH_3	Cl	CF_3	*i*-Pr	Br	Cl	I	Br	*i*-Pr	Cl
CH_3	Cl	CF_3	*t*-Bu	Br	Cl	I	Br	*t*-Bu	Cl
CH_3	Cl	Cl	Me	Cl	Cl	I	Br	Me	Br
CH_3	Cl	Cl	Et	Cl	Cl	I	Br	Et	Br
CH_3	Cl	Cl	*i*-Pr	Cl	Cl	I	Br	*i*-Pr	Br
CH_3	Cl	Cl	*t*-Bu	Cl	Cl	I	Br	*t*-Bu	Br
CH_3	Cl	Cl	Me	Br	Cl	CF_3	CF_3	Me	Cl
CH_3	Cl	Cl	Et	Br	Cl	CF_3	CF_3	Et	Cl
CH_3	Cl	Cl	*i*-Pr	Br	Cl	CF_3	CF_3	*i*-Pr	Cl
CH_3	Cl	Cl	*t*-Bu	Br	Cl	CF_3	CF_3	*t*-Bu	Cl
CH_3	Cl	Br	Me	Cl	Cl	CF_3	CF_3	Me	Br
CH_3	Cl	Br	Et	Cl	Cl	CF_3	CF_3	Et	Br

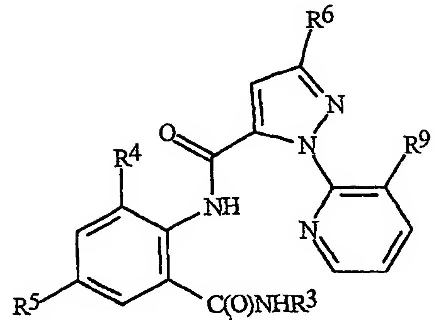
R^4	R^5	R^6	R^3	R^9	R^4	R^5	R^6	R^3	R^9
CH_3	Cl	Br	*i*-Pr	Cl	Cl	CF_3	CF_3	*i*-Pr	Br
CH_3	Cl	Br	*t*-Bu	Cl	Cl	CF_3	CF_3	*t*-Bu	Br
CH_3	Cl	Br	Me	Br	Cl	CF_3	Cl	Me	Cl
CH_3	Cl	Br	Et	Br	Cl	CF_3	Cl	Et	Cl
CH_3	Cl	Br	*i*-Pr	Br	Cl	CF_3	Cl	*i*-Pr	Cl
CH_3	Cl	Br	*t*-Bu	Br	Cl	CF_3	Cl	*t*-Bu	Cl
CH_3	Br	CF_3	Me	Cl	Cl	CF_3	Cl	Me	Br
CH_3	Br	CF_3	Et	Cl	Cl	CF_3	Cl	Et	Br
CH_3	Br	CF_3	*i*-Pr	Cl	Cl	CF_3	Cl	*i*-Pr	Br
CH_3	Br	CF_3	*t*-Bu	Cl	Cl	CF_3	Cl	*t*-Bu	Br
CH_3	Br	CF_3	Me	Br	Cl	CF_3	Br	Me	Cl
CH_3	Br	CF_3	Et	Br	Cl	CF_3	Br	Et	Cl
CH_3	Br	CF_3	*i*-Pr	Br	Cl	CF_3	Br	*i*-Pr	Cl
CH_3	Br	CF_3	*t*-Bu	Br	Cl	CF_3	Br	*t*-Bu	Cl
CH_3	Br	Cl	Me	Cl	Cl	CF_3	Br	Me	Br
CH_3	Br	Cl	Et	Cl	Cl	CF_3	Br	Et	Br
CH_3	Br	Cl	*i*-Pr	Cl	Cl	CF_3	Br	*i*-Pr	Br
CH_3	Br	Cl	*t*-Bu	Cl	Cl	CF_3	Br	*t*-Bu	Br
CH_3	Br	Cl	Me	Br	Cl	Cl	Cl	*n*-Pr	Cl
CH_3	Br	Cl	Et	Br	Cl	Cl	Cl	*n*-Bu	Cl
CH_3	Br	Cl	*i*-Pr	Br	Cl	Cl	Cl	*s*-Bu	Cl
CH_3	Br	Cl	*t*-Bu	Br	Cl	Cl	Cl	*i*-Bu	Cl
CH_3	Br	Br	Me	Cl	Br	F	CF_3	Me	Cl
CH_3	Br	Br	Et	Cl	Br	F	CF_3	Et	Cl
CH_3	Br	Br	*i*-Pr	Cl	Br	F	CF_3	*i*-Pr	Cl
CH_3	Br	Br	*t*-Bu	Cl	Br	F	CF_3	*t*-Bu	Cl
CH_3	Br	Br	Me	Br	Br	F	CF_3	Me	Br
CH_3	Br	Br	Et	Br	Br	F	CF_3	Et	Br
CH_3	Br	Br	*i*-Pr	Br	Br	F	CF_3	*i*-Pr	Br
CH_3	Br	Br	*t*-Bu	Br	Br	F	CF_3	*t*-Bu	Br
CH_3	I	CF_3	Me	Cl	Br	F	Cl	Me	Cl
CH_3	I	CF_3	Et	Cl	Br	F	Cl	Et	Cl
CH_3	I	CF_3	*i*-Pr	Cl	Br	F	Cl	*i*-Pr	Cl
CH_3	I	CF_3	*t*-Bu	Cl	Br	F	Cl	*t*-Bu	Cl
CH_3	I	CF_3	Me	Br	Br	F	Cl	Me	Br
CH_3	I	CF_3	Et	Br	Br	F	Cl	Et	Br
CH_3	I	CF_3	*i*-Pr	Br	Br	F	Cl	*i*-Pr	Br

R^4	R^5	R^6	R^3	R^9	R^4	R^5	R^6	R^3	R^9
CH_3	I	CF_3	*t*-Bu	Br	Br	F	Cl	*t*-Bu	Br
CH_3	I	Cl	Me	Cl	Br	F	Br	Me	Cl
CH_3	I	Cl	Et	Cl	Br	F	Br	Et	Cl
CH_3	I	Cl	*i*-Pr	Cl	Br	F	Br	*i*-Pr	Cl
CH_3	I	Cl	*t*-Bu	Cl	Br	F	Br	*t*-Bu	Cl
CH_3	I	Cl	Me	Br	Br	F	Br	Me	Br
CH_3	I	Cl	Et	Br	Br	F	Br	Et	Br
CH_3	I	Cl	*i*-Pr	Br	Br	F	Br	*i*-Pr	Br
CH_3	I	Cl	*t*-Bu	Br	Br	F	Br	*t*-Bu	Br
CH_3	I	Br	Me	Cl	Br	Cl	CF_3	Me	Cl
CH_3	I	Br	Et	Cl	Br	Cl	CF_3	Et	Cl
CH_3	I	Br	*i*-Pr	Cl	Br	Cl	CF_3	*i*-Pr	Cl
CH_3	I	Br	*t*-Bu	Cl	Br	Cl	CF_3	*t*-Bu	Cl
CH_3	I	Br	Me	Br	Br	Cl	CF_3	Me	Br
CH_3	I	Br	Et	Br	Br	Cl	CF_3	Et	Br
CH_3	I	Br	*i*-Pr	Br	Br	Cl	CF_3	*i*-Pr	Br
CH_3	I	Br	*t*-Bu	Br	Br	Cl	CF_3	*t*-Bu	Br
CH_3	CF_3	CF_3	Me	Cl	Br	Cl	Cl	Me	Cl
CH_3	CF_3	CF_3	Et	Cl	Br	Cl	Cl	Et	Cl
CH_3	CF_3	CF_3	*i*-Pr	Cl	Br	Cl	Cl	*i*-Pr	Cl
CH_3	CF_3	CF_3	*t*-Bu	Cl	Br	Cl	Cl	*t*-Bu	Cl
CH_3	CF_3	CF_3	Me	Br	Br	Cl	Cl	Me	Br
CH_3	CF_3	CF_3	Et	Br	Br	Cl	Cl	Et	Br
CH_3	CF_3	CF_3	*i*-Pr	Br	Br	Cl	Cl	*i*-Pr	Br
CH_3	CF_3	CF_3	*t*-Bu	Br	Br	Cl	Cl	*t*-Bu	Br
CH_3	CF_3	Cl	Me	Cl	Br	Cl	Br	Me	Cl
CH_3	CF_3	Cl	Et	Cl	Br	Cl	Br	Et	Cl
CH_3	CF_3	Cl	*i*-Pr	Cl	Br	Cl	Br	*i*-Pr	Cl
CH_3	CF_3	Cl	*t*-Bu	Cl	Br	Cl	Br	*t*-Bu	Cl
CH_3	CF_3	Cl	Me	Br	Br	Cl	Br	Me	Br
CH_3	CF_3	Cl	Et	Br	Br	Cl	Br	Et	Br
CH_3	CF_3	Cl	*i*-Pr	Br	Br	Cl	Br	*i*-Pr	Br
CH_3	CF_3	Cl	*t*-Bu	Br	Br	Cl	Br	*t*-Bu	Br
CH_3	CF_3	Br	Me	Cl	Br	Br	CF_3	Me	Cl
CH_3	CF_3	Br	Et	Cl	Br	Br	CF_3	Et	Cl
CH_3	CF_3	Br	*i*-Pr	Cl	Br	Br	CF_3	*i*-Pr	Cl
CH_3	CF_3	Br	*t*-Bu	Cl	Br	Br	CF_3	*t*-Bu	Cl

R^4	R^5	R^6	R^3	R^9	R^4	R^5	R^6	R^3	R^9
CH_3	CF_3	Br	Me	Br	Br	Br	CF_3	Me	Br
CH_3	CF_3	Br	Et	Br	Br	Br	CF_3	Et	Br
CH_3	CF_3	Br	*i*-Pr	Br	Br	Br	CF_3	*i*-Pr	Br
CH_3	CF_3	Br	*t*-Bu	Br	Br	Br	CF_3	*t*-Bu	Br
CH_3	Cl	Cl	*n*-Pr	Cl	Br	Br	Cl	Me	Cl
CH_3	Cl	Cl	*n*-Bu	Cl	Br	Br	Cl	Et	Cl
CH_3	Cl	Cl	*s*-Bu	Cl	Br	Br	Cl	*i*-Pr	Cl
CH_3	Cl	Cl	*i*-Bu	Cl	Br	Br	Cl	*t*-Bu	Cl
Cl	F	CF_3	Me	Cl	Br	Br	Cl	Me	Br
Cl	F	CF_3	Et	Cl	Br	Br	Cl	Et	Br
Cl	F	CF_3	*i*-Pr	Cl	Br	Br	Cl	*i*-Pr	Br
Cl	F	CF_3	*t*-Bu	Cl	Br	Br	Cl	*t*-Bu	Br
Cl	F	CF_3	Me	Br	Br	Br	Br	Me	Cl
Cl	F	CF_3	Et	Br	Br	Br	Br	Et	Cl
Cl	F	CF_3	*i*-Pr	Br	Br	Br	Br	*i*-Pr	Cl
Cl	F	CF_3	*t*-Bu	Br	Br	Br	Br	*t*-Bu	Cl
Cl	F	Cl	Me	Cl	Br	Br	Br	Me	Br
Cl	F	Cl	Et	Cl	Br	Br	Br	Et	Br
Cl	F	Cl	*i*-Pr	Cl	Br	Br	Br	*i*-Pr	Br
Cl	F	Cl	*t*-Bu	Cl	Br	Br	Br	*t*-Bu	Br
Cl	F	Cl	Me	Br	Br	I	CF_3	Me	Cl
Cl	F	Cl	Et	Br	Br	I	CF_3	Et	Cl
Cl	F	Cl	*i*-Pr	Br	Br	I	CF_3	*i*-Pr	Cl
Cl	F	Cl	*t*-Bu	Br	Br	I	CF_3	*t*-Bu	Cl
Cl	F	Br	Me	Cl	Br	I	CF_3	Me	Br
Cl	F	Br	Et	Cl	Br	I	CF_3	Et	Br
Cl	F	Br	*i*-Pr	Cl	Br	I	CF_3	*i*-Pr	Br
Cl	F	Br	*t*-Bu	Cl	Br	I	CF_3	*t*-Bu	Br
Cl	F	Br	Me	Br	Br	I	Cl	Me	Cl
Cl	F	Br	Et	Br	Br	I	Cl	Et	Cl
Cl	F	Br	*i*-Pr	Br	Br	I	Cl	*i*-Pr	Cl
Cl	F	Br	*t*-Bu	Br	Br	I	Cl	*t*-Bu	Cl
Cl	Cl	CF_3	Me	Cl	Br	I	Cl	Me	Br
Cl	Cl	CF_3	Et	Cl	Br	I	Cl	Et	Br
Cl	Cl	CF_3	*i*-Pr	Cl	Br	I	Cl	*i*-Pr	Br
Cl	Cl	CF_3	*t*-Bu	Cl	Br	I	Cl	*t*-Bu	Br
Cl	Cl	CF_3	Me	Br	Br	I	Br	Me	Cl

R^4	R^5	R^6	R^3	R^9	R^4	R^5	R^6	R^3	R^9
Cl	Cl	CF_3	Et	Br	Br	I	Br	Et	Cl
Cl	Cl	CF_3	*i*-Pr	Br	Br	I	Br	*i*-Pr	Cl
Cl	Cl	CF_3	*t*-Bu	Br	Br	I	Br	*t*-Bu	Cl
Cl	Cl	Cl	Me	Cl	Br	I	Br	Me	Br
Cl	Cl	Cl	Et	Cl	Br	I	Br	Et	Br
Cl	Cl	Cl	*i*-Pr	Cl	Br	I	Br	*i*-Pr	Br
Cl	Cl	Cl	*t*-Bu	Cl	Br	I	Br	*t*-Bu	Br
Cl	Cl	Cl	Me	Br	Br	CF_3	CF_3	Me	Cl
Cl	Cl	Cl	Et	Br	Br	CF_3	CF_3	Et	Cl
Cl	Cl	Cl	*i*-Pr	Br	Br	CF_3	CF_3	*i*-Pr	Cl
Cl	Cl	Cl	*t*-Bu	Br	Br	CF_3	CF_3	*t*-Bu	Cl
Cl	Cl	Br	Me	Cl	Br	CF_3	CF_3	Me	Br
Cl	Cl	Br	Et	Cl	Br	CF_3	CF_3	Et	Br
Cl	Cl	Br	*i*-Pr	Cl	Br	CF_3	CF_3	*i*-Pr	Br
Cl	Cl	Br	*t*-Bu	Cl	Br	CF_3	CF_3	*t*-Bu	Br
Cl	Cl	Br	Me	Br	Br	CF_3	Cl	Me	Cl
Cl	Cl	Br	Et	Br	Br	CF_3	Cl	Et	Cl
Cl	Cl	Br	*i*-Pr	Br	Br	CF_3	Cl	*i*-Pr	Cl
Cl	Cl	Br	*t*-Bu	Br	Br	CF_3	Cl	*t*-Bu	Cl
Cl	Br	CF_3	Me	Cl	Br	CF_3	Cl	Me	Br
Cl	Br	CF_3	Et	Cl	Br	CF_3	Cl	Et	Br
Cl	Br	CF_3	*i*-Pr	Cl	Br	CF_3	Cl	*i*-Pr	Br
Cl	Br	CF_3	*t*-Bu	Cl	Br	CF_3	Cl	*t*-Bu	Br
Cl	Br	CF_3	Me	Br	Br	CF_3	Br	Me	Cl
Cl	Br	CF_3	Et	Br	Br	CF_3	Br	Et	Cl
Cl	Br	CF_3	*i*-Pr	Br	Br	CF_3	Br	*i*-Pr	Cl
Cl	Br	CF_3	*t*-Bu	Br	Br	CF_3	Br	*t*-Bu	Cl
Cl	Br	Cl	Me	Cl	Br	CF_3	Br	Me	Br
Cl	Br	Cl	Et	Cl	Br	CF_3	Br	Et	Br
Cl	Br	Cl	*i*-Pr	Cl	Br	CF_3	Br	*i*-Pr	Br
Cl	Br	Cl	*t*-Bu	Cl	Br	CF_3	Br	*t*-Bu	Br

TABLE 6



R^4	R^5	R^6	R^3	R^9	R^4	R^5	R^6	R^3	R^9
CH_3	F	CF_3	Me	Cl	Cl	Br	Cl	Me	Br
CH_3	F	CF_3	Et	Cl	Cl	Br	Cl	Et	Br
CH_3	F	CF_3	*i*-Pr	Cl	Cl	Br	Cl	*i*-Pr	Br
CH_3	F	CF_3	*t*-Bu	Cl	Cl	Br	Cl	*t*-Bu	Br
CH_3	F	CF_3	Me	Br	Cl	Br	Br	Me	Cl
CH_3	F	CF_3	Et	Br	Cl	Br	Br	Et	Cl
CH_3	F	CF_3	*i*-Pr	Br	Cl	Br	Br	*i*-Pr	Cl
CH_3	F	CF_3	*t*-Bu	Br	Cl	Br	Br	*t*-Bu	Cl
CH_3	F	Cl	Me	Cl	Cl	Br	Br	Me	Br
CH_3	F	Cl	Et	Cl	Cl	Br	Br	Et	Br
CH_3	F	Cl	*i*-Pr	Cl	Cl	Br	Br	*i*-Pr	Br
CH_3	F	Cl	*t*-Bu	Cl	Cl	Br	Br	*t*-Bu	Br
CH_3	F	Cl	Me	Br	Cl	I	CF_3	Me	Cl
CH_3	F	Cl	Et	Br	Cl	I	CF_3	Et	Cl
CH_3	F	Cl	*i*-Pr	Br	Cl	I	CF_3	*i*-Pr	Cl
CH_3	F	Cl	*t*-Bu	Br	Cl	I	CF_3	*t*-Bu	Cl
CH_3	F	Br	Me	Cl	Cl	I	CF_3	Me	Br
CH_3	F	Br	Et	Cl	Cl	I	CF_3	Et	Br
CH_3	F	Br	*i*-Pr	Cl	Cl	I	CF_3	*i*-Pr	Br
CH_3	F	Br	*t*-Bu	Cl	Cl	I	CF_3	*t*-Bu	Br
CH_3	F	Br	Me	Br	Cl	I	Cl	Me	Cl
CH_3	F	Br	Et	Br	Cl	I	Cl	Et	Cl
CH_3	F	Br	*i*-Pr	Br	Cl	I	Cl	*i*-Pr	Cl
CH_3	F	Br	*t*-Bu	Br	Cl	I	Cl	*t*-Bu	Cl
CH_3	Cl	CF_3	Me	Cl	Cl	I	Cl	Me	Br
CH_3	Cl	CF_3	Et	Cl	Cl	I	Cl	Et	Br
CH_3	Cl	CF_3	*i*-Pr	Cl	Cl	I	Cl	*i*-Pr	Br
CH_3	Cl	CF_3	*t*-Bu	Cl	Cl	I	Cl	*t*-Bu	Br

R^4	R^5	R^6	R^3	R^9	R^4	R^5	R^6	R^3	R^9
CH_3	Cl	CF_3	Me	Br	Cl	I	Br	Me	Cl
CH_3	Cl	CF_3	Et	Br	Cl	I	Br	Et	Cl
CH_3	Cl	CF_3	*i*-Pr	Br	Cl	I	Br	*i*-Pr	Cl
CH_3	Cl	CF_3	*t*-Bu	Br	Cl	I	Br	*t*-Bu	Cl
CH_3	Cl	Cl	Me	Cl	Cl	I	Br	Me	Br
CH_3	Cl	Cl	Et	Cl	Cl	I	Br	Et	Br
CH_3	Cl	Cl	*i*-Pr	Cl	Cl	I	Br	*i*-Pr	Br
CH_3	Cl	Cl	*t*-Bu	Cl	Cl	I	Br	*t*-Bu	Br
CH_3	Cl	Cl	Me	Br	Cl	CF_3	CF_3	Me	Cl
CH_3	Cl	Cl	Et	Br	Cl	CF_3	CF_3	Et	Cl
CH_3	Cl	Cl	*i*-Pr	Br	Cl	CF_3	CF_3	*i*-Pr	Cl
CH_3	Cl	Cl	*t*-Bu	Br	Cl	CF_3	CF_3	*t*-Bu	Cl
CH_3	Cl	Br	Me	Cl	Cl	CF_3	CF_3	Me	Br
CH_3	Cl	Br	Et	Cl	Cl	CF_3	CF_3	Et	Br
CH_3	Cl	Br	*i*-Pr	Cl	Cl	CF_3	CF_3	*i*-Pr	Br
CH_3	Cl	Br	*t*-Bu	Cl	Cl	CF_3	CF_3	*t*-Bu	Br
CH_3	Cl	Br	Me	Br	Cl	CF_3	Cl	Me	Cl
CH_3	Cl	Br	Et	Br	Cl	CF_3	Cl	Et	Cl
CH_3	Cl	Br	*i*-Pr	Br	Cl	CF_3	Cl	*i*-Pr	Cl
CH_3	Cl	Br	*t*-Bu	Br	Cl	CF_3	Cl	*t*-Bu	Cl
CH_3	Br	CF_3	Me	Cl	Cl	CF_3	Cl	Me	Br
CH_3	Br	CF_3	Et	Cl	Cl	CF_3	Cl	Et	Br
CH_3	Br	CF_3	*i*-Pr	Cl	Cl	CF_3	Cl	*i*-Pr	Br
CH_3	Br	CF_3	*t*-Bu	Cl	Cl	CF_3	Cl	*t*-Bu	Br
CH_3	Br	CF_3	Me	Br	Cl	CF_3	Br	Me	Cl
CH_3	Br	CF_3	Et	Br	Cl	CF_3	Br	Et	Cl
CH_3	Br	CF_3	*i*-Pr	Br	Cl	CF_3	Br	*i*-Pr	Cl
CH_3	Br	CF_3	*t*-Bu	Br	Cl	CF_3	Br	*t*-Bu	Cl
CH_3	Br	Cl	Me	Cl	Cl	CF_3	Br	Me	Br
CH_3	Br	Cl	Et	Cl	Cl	CF_3	Br	Et	Br
CH_3	Br	Cl	*i*-Pr	Cl	Cl	CF_3	Br	*i*-Pr	Br
CH_3	Br	Cl	*t*-Bu	Cl	Cl	CF_3	Br	*t*-Bu	Br
CH_3	Br	Cl	Me	Br	Cl	Cl	Cl	*n*-Pr	Cl
CH_3	Br	Cl	Et	Br	Cl	Cl	Cl	*n*-Bu	Cl
CH_3	Br	Cl	*i*-Pr	Br	Cl	Cl	Cl	*s*-Bu	Cl
CH_3	Br	Cl	*t*-Bu	Br	Cl	Cl	Cl	*i*-Bu	Cl
CH_3	Br	Br	Me	Cl	Br	F	CF_3	Me	Cl

$\underline{R^4}$	$\underline{R^5}$	$\underline{R^6}$	$\underline{R^3}$	$\underline{R^9}$	$\underline{R^4}$	$\underline{R^5}$	$\underline{R^6}$	$\underline{R^3}$	$\underline{R^9}$
CH_3	Br	Br	Et	Cl	Br	F	CF_3	Et	Cl
CH_3	Br	Br	*i*-Pr	Cl	Br	F	CF_3	*i*-Pr	Cl
CH_3	Br	Br	*t*-Bu	Cl	Br	F	CF_3	*t*-Bu	Cl
CH_3	Br	Br	Me	Br	Br	F	CF_3	Me	Br
CH_3	Br	Br	Et	Br	Br	F	CF_3	Et	Br
CH_3	Br	Br	*i*-Pr	Br	Br	F	CF_3	*i*-Pr	Br
CH_3	Br	Br	*t*-Bu	Br	Br	F	CF_3	*t*-Bu	Br
CH_3	I	CF_3	Me	Cl	Br	F	Cl	Me	Cl
CH_3	I	CF_3	Et	Cl	Br	F	Cl	Et	Cl
CH_3	I	CF_3	*i*-Pr	Cl	Br	F	Cl	*i*-Pr	Cl
CH_3	I	CF_3	*t*-Bu	Cl	Br	F	Cl	*t*-Bu	Cl
CH_3	I	CF_3	Me	Br	Br	F	Cl	Me	Br
CH_3	I	CF_3	Et	Br	Br	F	Cl	Et	Br
CH_3	I	CF_3	*i*-Pr	Br	Br	F	Cl	*i*-Pr	Br
CH_3	I	CF_3	*t*-Bu	Br	Br	F	Cl	*t*-Bu	Br
CH_3	I	Cl	Me	Cl	Br	F	Br	Me	Cl
CH_3	I	Cl	Et	Cl	Br	F	Br	Et	Cl
CH_3	I	Cl	*i*-Pr	Cl	Br	F	Br	*i*-Pr	Cl
CH_3	I	Cl	*t*-Bu	Cl	Br	F	Br	*t*-Bu	Cl
CH_3	I	Cl	Me	Br	Br	F	Br	Me	Br
CH_3	I	Cl	Et	Br	Br	F	Br	Et	Br
CH_3	I	Cl	*i*-Pr	Br	Br	F	Br	*i*-Pr	Br
CH_3	I	Cl	*t*-Bu	Br	Br	F	Br	*t*-Bu	Br
CH_3	I	Br	Me	Cl	Br	Cl	CF_3	Me	Cl
CH_3	I	Br	Et	Cl	Br	Cl	CF_3	Et	Cl
CH_3	I	Br	*i*-Pr	Cl	Br	Cl	CF_3	*i*-Pr	Cl
CH_3	I	Br	*t*-Bu	Cl	Br	Cl	CF_3	*t*-Bu	Cl
CH_3	I	Br	Me	Br	Br	Cl	CF_3	Me	Br
CH_3	I	Br	Et	Br	Br	Cl	CF_3	Et	Br
CH_3	I	Br	*i*-Pr	Br	Br	Cl	CF_3	*i*-Pr	Br
CH_3	I	Br	*t*-Bu	Br	Br	Cl	CF_3	*t*-Bu	Br
CH_3	CF_3	CF_3	Me	Cl	Br	Cl	Cl	Me	Cl
CH_3	CF_3	CF_3	Et	Cl	Br	Cl	Cl	Et	Cl
CH_3	CF_3	CF_3	*i*-Pr	Cl	Br	Cl	Cl	*i*-Pr	Cl
CH_3	CF_3	CF_3	*t*-Bu	Cl	Br	Cl	Cl	*t*-Bu	Cl
CH_3	CF_3	CF_3	Me	Br	Br	Cl	Cl	Me	Br
CH_3	CF_3	CF_3	Et	Br	Br	Cl	Cl	Et	Br

R^4	R^5	R^6	R^3	R^9
CH_3	CF_3	CF_3	*i*-Pr	Br
CH_3	CF_3	CF_3	*t*-Bu	Br
CH_3	CF_3	Cl	Me	Cl
CH_3	CF_3	Cl	Et	Cl
CH_3	CF_3	Cl	*i*-Pr	Cl
CH_3	CF_3	Cl	*t*-Bu	Cl
CH_3	CF_3	Cl	Me	Br
CH_3	CF_3	Cl	Et	Br
CH_3	CF_3	Cl	*i*-Pr	Br
CH_3	CF_3	Cl	*t*-Bu	Br
CH_3	CF_3	Br	Me	Cl
CH_3	CF_3	Br	Et	Cl
CH_3	CF_3	Br	*i*-Pr	Cl
CH_3	CF_3	Br	*t*-Bu	Cl
CH_3	CF_3	Br	Me	Br
CH_3	CF_3	Br	Et	Br
CH_3	CF_3	Br	*i*-Pr	Br
CH_3	CF_3	Br	*t*-Bu	Br
CH_3	Cl	Cl	*n*-Pr	Cl
CH_3	Cl	Cl	*n*-Bu	Cl
CH_3	Cl	Cl	*s*-Bu	Cl
CH_3	Cl	Cl	*i*-Bu	Cl
Cl	F	CF_3	Me	Cl
Cl	F	CF_3	Et	Cl
Cl	F	CF_3	*i*-Pr	Cl
Cl	F	CF_3	*t*-Bu	Cl
Cl	F	CF_3	Me	Br
Cl	F	CF_3	Et	Br
Cl	F	CF_3	*i*-Pr	Br
Cl	F	CF_3	*t*-Bu	Br
Cl	F	Cl	Me	Cl
Cl	F	Cl	Et	Cl
Cl	F	Cl	*i*-Pr	Cl
Cl	F	Cl	*t*-Bu	Cl
Cl	F	Cl	Me	Br
Cl	F	Cl	Et	Br
Cl	F	Cl	*i*-Pr	Br

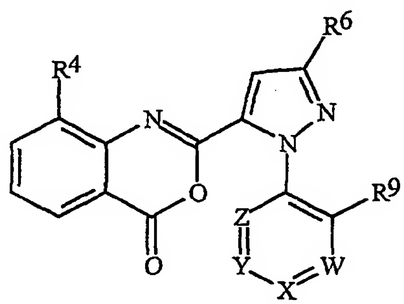
R^4	R^5	R^6	R^3	R^9
Br	Cl	Cl	*i*-Pr	Br
Br	Cl	Cl	*t*-Bu	Br
Br	Cl	Br	Me	Cl
Br	Cl	Br	Et	Cl
Br	Cl	Br	*i*-Pr	Cl
Br	Cl	Br	*t*-Bu	Cl
Br	Cl	Br	Me	Br
Br	Cl	Br	Et	Br
Br	Cl	Br	*i*-Pr	Br
Br	Cl	Br	*t*-Bu	Br
Br	Br	CF_3	Me	Cl
Br	Br	CF_3	Et	Cl
Br	Br	CF_3	*i*-Pr	Cl
Br	Br	CF_3	*t*-Bu	Cl
Br	Br	CF_3	Me	Br
Br	Br	CF_3	Et	Br
Br	Br	CF_3	*i*-Pr	Br
Br	Br	CF_3	*t*-Bu	Br
Br	Br	Cl	Me	Cl
Br	Br	Cl	Et	Cl
Br	Br	Cl	*i*-Pr	Cl
Br	Br	Cl	*t*-Bu	Cl
Br	Br	Cl	Me	Br
Br	Br	Cl	Et	Br
Br	Br	Cl	*i*-Pr	Br
Br	Br	Cl	*t*-Bu	Br
Br	Br	Br	Me	Cl
Br	Br	Br	Et	Cl
Br	Br	Br	*i*-Pr	Cl
Br	Br	Br	*t*-Bu	Cl
Br	Br	Br	Me	Br
Br	Br	Br	Et	Br
Br	Br	Br	*i*-Pr	Br
Br	Br	Br	*t*-Bu	Br
Br	I	CF_3	Me	Cl
Br	I	CF_3	Et	Cl
Br	I	CF_3	*i*-Pr	Cl

R^4	R^5	R^6	R^3	R^9	R^4	R^5	R^6	R^3	R^9
Cl	F	Cl	*t*-Bu	Br	Br	I	CF_3	*t*-Bu	Cl
Cl	F	Br	Me	Cl	Br	I	CF_3	Me	Br
Cl	F	Br	Et	Cl	Br	I	CF_3	Et	Br
Cl	F	Br	*i*-Pr	Cl	Br	I	CF_3	*i*-Pr	Br
Cl	F	Br	*t*-Bu	Cl	Br	I	CF_3	*t*-Bu	Br
Cl	F	Br	Me	Br	Br	I	Cl	Me	Cl
Cl	F	Br	Et	Br	Br	I	Cl	Et	Cl
Cl	F	Br	*i*-Pr	Br	Br	I	Cl	*i*-Pr	Cl
Cl	F	Br	*t*-Bu	Br	Br	I	Cl	*t*-Bu	Cl
Cl	Cl	CF_3	Me	Cl	Br	I	Cl	Me	Br
Cl	Cl	CF_3	Et	Cl	Br	I	Cl	Et	Br
Cl	Cl	CF_3	*i*-Pr	Cl	Br	I	Cl	*i*-Pr	Br
Cl	Cl	CF_3	*t*-Bu	Cl	Br	I	Cl	*t*-Bu	Br
Cl	Cl	CF_3	Me	Br	Br	I	Br	Me	Cl
Cl	Cl	CF_3	Et	Br	Br	I	Br	Et	Cl
Cl	Cl	CF_3	*i*-Pr	Br	Br	I	Br	*i*-Pr	Cl
Cl	Cl	CF_3	*t*-Bu	Br	Br	I	Br	*t*-Bu	Cl
Cl	Cl	Cl	Me	Cl	Br	I	Br	Me	Br
Cl	Cl	Cl	Et	Cl	Br	I	Br	Et	Br
Cl	Cl	Cl	*i*-Pr	Cl	Br	I	Br	*i*-Pr	Br
Cl	Cl	Cl	*t*-Bu	Cl	Br	I	Br	*t*-Bu	Br
Cl	Cl	Cl	Me	Br	Br	CF_3	CF_3	Me	Cl
Cl	Cl	Cl	Et	Br	Br	CF_3	CF_3	Et	Cl
Cl	Cl	Cl	*i*-Pr	Br	Br	CF_3	CF_3	*i*-Pr	Cl
Cl	Cl	Cl	*t*-Bu	Br	Br	CF_3	CF_3	*t*-Bu	Cl
Cl	Cl	Br	Me	Cl	Br	CF_3	CF_3	Me	Br
Cl	Cl	Br	Et	Cl	Br	CF_3	CF_3	Et	Br
Cl	Cl	Br	*i*-Pr	Cl	Br	CF_3	CF_3	*i*-Pr	Br
Cl	Cl	Br	*t*-Bu	Cl	Br	CF_3	CF_3	*t*-Bu	Br
Cl	Cl	Br	Me	Br	Br	CF_3	Cl	Me	Cl
Cl	Cl	Br	Et	Br	Br	CF_3	Cl	Et	Cl
Cl	Cl	Br	*i*-Pr	Br	Br	CF_3	Cl	*i*-Pr	Cl
Cl	Cl	Br	*t*-Bu	Br	Br	CF_3	Cl	*t*-Bu	Cl
Cl	Br	CF_3	Me	Cl	Br	CF_3	Cl	Me	Br
Cl	Br	CF_3	Et	Cl	Br	CF_3	Cl	Et	Br
Cl	Br	CF_3	*i*-Pr	Cl	Br	CF_3	Cl	*i*-Pr	Br
Cl	Br	CF_3	*t*-Bu	Cl	Br	CF_3	Cl	*t*-Bu	Br

R^4	R^5	R^6	R^3	R^9	R^4	R^5	R^6	R^3	R^9
Cl	Br	CF_3	Me	Br	Br	CF_3	Br	Me	Cl
Cl	Br	CF_3	Et	Br	Br	CF_3	Br	Et	Cl
Cl	Br	CF_3	*i*-Pr	Br	Br	CF_3	Br	*i*-Pr	Cl
Cl	Br	CF_3	*t*-Bu	Br	Br	CF_3	Br	*t*-Bu	Cl
Cl	Br	Cl	Me	Cl	Br	CF_3	Br	Me	Br
Cl	Br	Cl	Et	Cl	Br	CF_3	Br	Et	Br
Cl	Br	Cl	*i*-Pr	Cl	Br	CF_3	Br	*i*-Pr	Br
Cl	Br	Cl	*t*-Bu	Cl	Br	CF_3	Br	*t*-Bu	Br

As shown in Scheme 7 and further illustrated in Examples 4 and 5, the benzoxazines of Formula **10a-b** such as those listed in Tables 7 and 8 are useful for preparing the compounds of Formula **I**, including those listed in Tables 2 and 5.

Table 7



10a

W	X	Y	Z	R^4	R^6	R^9
CH	CH	CH	CH	Me	CF_3	Me
CH	CH	CH	CH	Cl	CF_3	Me
CH	CH	CH	CH	Br	CF_3	Me
CH	CH	CH	CH	Me	Cl	Me
CH	CH	CH	CH	Cl	Cl	Me
CH	CH	CH	CH	Br	Cl	Me
CH	CH	CH	CH	Me	Br	Me
CH	CH	CH	CH	Cl	Br	Me
CH	CH	CH	CH	Br	Br	Me
CH	CH	CH	CH	Me	CN	Me
CH	CH	CH	CH	Cl	CN	Me
CH	CH	CH	CH	Br	CN	Me

W	X	Y	Z	R^4	R^6	R^9
CH	CH	CH	CH	Me	CF_3	F
CH	CH	CH	CH	Cl	CF_3	F
CH	CH	CH	CH	Br	CF_3	F
CH	CH	CH	CH	Me	Cl	F
CH	CH	CH	CH	Cl	Cl	F
CH	CH	CH	CH	Br	Cl	F
CH	CH	CH	CH	Me	Br	F
CH	CH	CH	CH	Cl	Br	F
CH	CH	CH	CH	Br	Br	F
CH	CH	CH	CH	Me	CN	F
CH	CH	CH	CH	Cl	CN	F
CH	CH	CH	CH	Br	CN	F
CH	CH	CH	CH	Me	CF_3	Cl
CH	CH	CH	CH	Cl	CF_3	Cl
CH	CH	CH	CH	Br	CF_3	Cl
CH	CH	CH	CH	Me	Cl	Cl
CH	CH	CH	CH	Cl	Cl	Cl
CH	CH	CH	CH	Br	Cl	Cl
CH	CH	CH	CH	Me	Br	Cl
CH	CH	CH	CH	Cl	Br	Cl
CH	CH	CH	CH	Br	Br	Cl
CH	CH	CH	CH	Me	CN	Cl
CH	CH	CH	CH	Cl	CN	Cl
CH	CH	CH	CH	Br	CN	Cl
CH	CH	CH	CH	Me	CF_3	Br
CH	CH	CH	CH	Cl	CF_3	Br
CH	CH	CH	CH	Br	CF_3	Br
CH	CH	CH	CH	Me	Cl	Br
CH	CH	CH	CH	Cl	Cl	Br
CH	CH	CH	CH	Br	Cl	Br
CH	CH	CH	CH	Me	Br	Br
CH	CH	CH	CH	Cl	Br	Br
CH	CH	CH	CH	Br	Br	Br
CH	CH	CH	CH	Me	CN	Br
CH	CH	CH	CH	Cl	CN	Br
CH	CH	CH	CH	Br	CN	Br
CH	CH	CH	CH	Me	CF_3	CN

W	X	Y	Z	R^4	R^6	R^9
CH	CH	CH	CH	Cl	CF_3	CN
CH	CH	CH	CH	Br	CF_3	CN
CH	CH	CH	CH	Me	Cl	CN
CH	CH	CH	CH	Cl	Cl	CN
CH	CH	CH	CH	Br	Cl	CN
CH	CH	CH	CH	Me	Br	CN
CH	CH	CH	CH	Cl	Br	CN
CH	CH	CH	CH	Br	Br	CN
CH	CH	CH	CH	Me	CN	CN
CH	CH	CH	CH	Cl	CN	CN
CH	CH	CH	CH	Br	CN	CN
CH	CH	CH	N	Me	CF_3	Me
CH	CH	CH	N	Cl	CF_3	Me
CH	CH	CH	N	Br	CF_3	Me
CH	CH	CH	N	Me	Cl	Me
CH	CH	CH	N	Cl	Cl	Me
CH	CH	CH	N	Br	Cl	Me
CH	CH	CH	N	Me	Br	Me
CH	CH	CH	N	Cl	Br	Me
CH	CH	CH	N	Br	Br	Me
CH	CH	CH	N	Me	CN	Me
CH	CH	CH	N	Cl	CN	Me
CH	CH	CH	N	Br	CN	Me
CH	CH	CH	N	Me	CF_3	F
CH	CH	CH	N	Cl	CF_3	F
CH	CH	CH	N	Br	CF_3	F
CH	CH	CH	N	Me	Cl	F
CH	CH	CH	N	Cl	Cl	F
CH	CH	CH	N	Br	Cl	F
CH	CH	CH	N	Me	Br	F
CH	CH	CH	N	Cl	Br	F
CH	CH	CH	N	Br	Br	F
CH	CH	CH	N	Me	CN	F
CH	CH	CH	N	Cl	CN	F
CH	CH	CH	N	Br	CN	F
CH	CH	CH	N	Me	CF_3	Cl
CH	CH	CH	N	Cl	CF_3	Cl

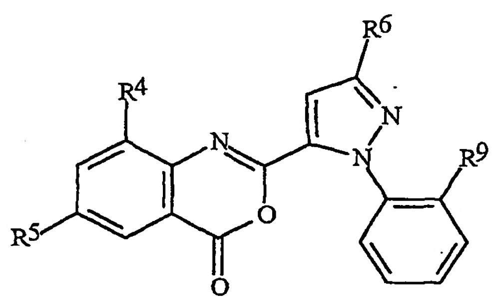
W	X	Y	Z	R^4	R^6	R^9
CH	CH	CH	N	Br	CF_3	Cl
CH	CH	CH	N	Me	Cl	Cl
CH	CH	CH	N	Cl	Cl	Cl
CH	CH	CH	N	Br	Cl	Cl
CH	CH	CH	N	Me	Br	Cl
CH	CH	CH	N	Cl	Br	Cl
CH	CH	CH	N	Br	Br	Cl
CH	CH	CH	N	Me	CN	Cl
CH	CH	CH	N	Cl	CN	Cl
CH	CH	CH	N	Br	CN	Cl
CH	CH	CH	N	Me	CF_3	Br
CH	CH	CH	N	Cl	CF_3	Br
CH	CH	CH	N	Br	CF_3	Br
CH	CH	CH	N	Me	Cl	Br
CH	CH	CH	N	Cl	Cl	Br
CH	CH	CH	N	Br	Cl	Br
CH	CH	CH	N	Me	Br	Br
CH	CH	CH	N	Cl	Br	Br
CH	CH	CH	N	Br	Br	Br
CH	CH	CH	N	Me	CN	Br
CH	CH	CH	N	Cl	CN	Br
CH	CH	CH	N	Br	CN	Br
CH	CH	CH	N	Me	CF_3	CN
CH	CH	CH	N	Cl	CF_3	CN
CH	CH	CH	N	Br	CF_3	CN
CH	CH	CH	N	Me	Cl	CN
CH	CH	CH	N	Cl	Cl	CN
CH	CH	CH	N	Br	Cl	CN
CH	CH	CH	N	Me	Br	CN
CH	CH	CH	N	Cl	Br	CN
CH	CH	CH	N	Br	Br	CN
CH	CH	CH	N	Me	CN	CN
CH	CH	CH	N	Cl	CN	CN
CH	CH	CH	N	Br	CN	CN
C-Cl	CH	CH	CH	Me	CF_3	Cl
C-F	CH	CH	CH	Me	CF_3	F
CH	CH	CH	CH	Me	CF_3	ethynyl

W	X	Y	Z	R^4	R^6	R^9
CH	CH	CH	CH	Me	CF_3	I
CH	CH	CH	CH	Me	CF_3	SO_2Me
C-Cl	CH	CH	CH	Cl	CF_3	Cl
C-F	CH	CH	CH	Cl	CF_3	F
CH	CH	CH	CH	Cl	CF_3	ethynyl
CH	CH	CH	CH	Cl	CF_3	I
CH	CH	CH	CH	Cl	CF_3	SO_2Me
C-Cl	CH	CH	CH	Me	Br	Cl
C-F	CH	CH	CH	Me	Br	F
CH	CH	CH	CH	Me	Br	ethynyl
CH	CH	CH	CH	Me	Br	I
CH	CH	CH	CH	Me	Br	SO_2Me
C-Cl	CH	CH	CH	Cl	Br	Cl
C-F	CH	CH	CH	Cl	Br	F
CH	CH	CH	CH	Cl	Br	ethynyl
CH	CH	CH	CH	Cl	Br	I
CH	CH	CH	CH	Cl	Br	SO_2Me
C-Cl	CH	CH	N	Me	CF_3	Cl
C-F	CH	CH	N	Me	CF_3	F
CH	CH	CH	N	Me	CF_3	ethynyl
CH	CH	CH	N	Me	CF_3	I
CH	CH	CH	N	Me	CF_3	SO_2Me
C-Cl	CH	CH	N	Cl	CF_3	Cl
C-F	CH	CH	N	Cl	CF_3	F
CH	CH	CH	N	Cl	CF_3	ethynyl
CH	CH	CH	N	Cl	CF_3	I
CH	CH	CH	N	Cl	CF_3	SO_2Me
C-Cl	CH	CH	N	Me	Br	Cl
C-F	CH	CH	N	Me	Br	F
CH	CH	CH	N	Me	Br	ethynyl
CH	CH	CH	N	Me	Br	I
CH	CH	CH	N	Me	Br	SO_2Me
C-Cl	CH	CH	N	Cl	Br	Cl
C-F	CH	CH	N	Cl	Br	F
CH	CH	CH	N	Cl	Br	ethynyl
CH	CH	CH	N	Cl	Br	I
CH	CH	CH	N	Cl	Br	SO_2Me

W	X	Y	Z	R4	R6	R9
CH	N	CH	N	Me	CF_3	H
CH	N	CH	N	Me	CF_3	Me
CH	N	CH	N	Me	CF_3	Cl
CH	N	CH	N	Cl	CF_3	H
CH	N	CH	N	Cl	CF_3	Me
CH	N	CH	N	Cl	CF_3	Cl
CH	N	CH	N	Me	CN	H
CH	N	CH	N	Me	CN	Me
CH	N	CH	N	Me	CN	Cl
CH	N	CH	N	Cl	CN	H
CH	N	CH	N	Cl	CN	Me
CH	N	CH	N	Cl	CN	Cl
CH	N	CH	N	Me	Br	H
CH	N	CH	N	Me	Br	Me
CH	N	CH	N	Me	Br	Cl
CH	N	CH	N	Cl	Br	H
CH	N	CH	N	Cl	Br	Me
CH	N	CH	N	Cl	Br	Cl
CH	CH	N	N	Me	CF_3	H
CH	CH	N	N	Me	CF_3	Me
CH	CH	N	N	Me	CF_3	Cl
CH	CH	N	N	Cl	CF_3	H
CH	CH	N	N	Cl	CF_3	Me
CH	CH	N	N	Cl	CF_3	Cl
CH	CH	N	N	Me	CN	H
CH	CH	N	N	Me	CN	Me
CH	CH	N	N	Me	CN	Cl
CH	CH	N	N	Cl	CN	H
CH	CH	N	N	Cl	CN	Me
CH	CH	N	N	Cl	CN	Cl
CH	CH	N	N	Me	Br	H
CH	CH	N	N	Me	Br	Me
CH	CH	N	N	Me	Br	Cl
CH	CH	N	N	Cl	Br	H
CH	CH	N	N	Cl	Br	Me
CH	CH	N	N	Cl	Br	Cl
CH	CH	N	N	Me	CF_3	H

W	X	Y	Z	R^4	R^6	R^9
CH	CH	N	N	Me	CF_3	Me
CH	CH	N	N	Me	CF_3	Cl
CH	CH	N	N	Cl	CF_3	H
CH	CH	N	N	Cl	CF_3	Me
CH	CH	N	N	Cl	CF_3	Cl
CH	CH	N	N	Me	CN	H
CH	CH	N	N	Me	CN	Me
CH	CH	N	N	Me	CN	Cl
CH	CH	N	N	Cl	CN	H
CH	CH	N	N	Cl	CN	Me
CH	CH	N	N	Cl	CN	Cl
CH	CH	N	N	Me	Br	H
CH	CH	N	N	Me	Br	Me
CH	CH	N	N	Me	Br	Cl
CH	CH	N	N	Cl	Br	H
CH	CH	N	N	Cl	Br	Me
CH	CH	N	N	Cl	Br	Cl

TABLE 8



10b

R^4	R^5	R^6	R^9	R^4	R^5	R^6	R^9
CH_3	F	CF_3	Cl	Cl	Br	Cl	Br
CH_3	F	CF_3	Br	Cl	Br	Br	Cl
CH_3	F	Cl	Cl	Cl	Br	Br	Br
CH_3	F	Cl	Br	Cl	I	CF_3	Cl
CH_3	F	Br	Cl	Cl	I	CF_3	Br
CH_3	F	Br	Br	Cl	I	Cl	Cl
CH_3	Cl	CF_3	Cl	Cl	I	Cl	Br
CH_3	Cl	CF_3	Br	Cl	I	Br	Cl
CH_3	Cl	Cl	Cl	Cl	I	Br	Br

R^4	R^5	R^6	R^9	R^4	R^5	R^6	R^9
CH_3	Cl	Cl	Br	Cl	CF_3	CF_3	Cl
CH_3	Cl	Br	Cl	Cl	CF_3	CF_3	Br
CH_3	Cl	Br	Br	Cl	CF_3	Cl	Cl
CH_3	Br	CF_3	Cl	Cl	CF_3	Cl	Br
CH_3	Br	CF_3	Br	Cl	CF_3	Br	Cl
CH_3	Br	Cl	Cl	Cl	CF_3	Br	Br
CH_3	Br	Cl	Br	Cl	Cl	Cl	Cl
CH_3	Br	Br	Cl	Br	F	CF_3	Cl
CH_3	Br	Br	Br	Br	F	CF_3	Br
CH_3	I	CF_3	Cl	Br	F	Cl	Cl
CH_3	I	CF_3	Br	Br	F	Cl	Br
CH_3	I	Cl	Cl	Br	F	Br	Cl
CH_3	I	Cl	Br	Br	F	Br	Br
CH_3	I	Br	Cl	Br	Cl	CF_3	Cl
CH_3	I	Br	Br	Br	Cl	CF_3	Br
CH_3	CF_3	CF_3	Cl	Br	Cl	Cl	Cl
CH_3	CF_3	CF_3	Br	Br	Cl	Cl	Br
CH_3	CF_3	Cl	Cl	Br	Cl	Br	Cl
CH_3	CF_3	Cl	Br	Br	Cl	Br	Br
CH_3	CF_3	Br	Cl	Br	Br	CF_3	Cl
CH_3	CF_3	Br	Br	Br	Br	CF_3	Br
CH_3	Cl	Cl	Cl	Br	Br	Cl	Cl
Cl	F	CF_3	Cl	Br	Br	Cl	Br
Cl	F	CF_3	Br	Br	Br	Br	Cl
Cl	F	Cl	Cl	Br	Br	Br	Br
Cl	F	Cl	Br	Br	I	CF_3	Cl
Cl	F	Br	Cl	Br	I	CF_3	Br
Cl	F	Br	Br	Br	I	Cl	Cl
Cl	Cl	CF_3	Cl	Br	I	Cl	Br
Cl	Cl	CF_3	Br	Br	I	Br	Cl
Cl	Cl	Cl	Cl	Br	I	Br	Br
Cl	Cl	Cl	Br	Br	CF_3	CF_3	Cl
Cl	Cl	Br	Cl	Br	CF_3	CF_3	Br
Cl	Cl	Br	Br	Br	CF_3	Cl	Cl
Cl	Br	CF_3	Cl	Br	CF_3	Cl	Br
Cl	Br	CF_3	Br	Br	CF_3	Br	Cl
Cl	Br	Cl	Cl	Br	CF_3	Br	Br

Formulation/Utility

Compounds of this invention will generally be used as a formulation or composition with an agriculturally suitable carrier comprising at least one of a liquid diluent, a solid diluent or a surfactant. The formulation or composition ingredients are selected to be consistent with the physical properties of the active ingredient, mode of application and environmental factors such as soil type, moisture and temperature. Useful formulations include liquids such as solutions (including emulsifiable concentrates), suspensions, emulsions (including microemulsions and/or suspoemulsions) and the like which optionally can be thickened into gels. Useful formulations further include solids such as dusts, powders, granules, pellets, tablets, films, and the like which can be water-dispersible ("wettable") or water-soluble. Active ingredient can be (micro)encapsulated and further formed into a suspension or solid formulation; alternatively the entire formulation of active ingredient can be encapsulated (or "overcoated"). Encapsulation can control or delay release of the active ingredient. Sprayable formulations can be extended in suitable media and used at spray volumes from about one to several hundred liters per hectare. High-strength compositions are primarily used as intermediates for further formulation.

The formulations will typically contain effective amounts of active ingredient, diluent and surfactant within the following approximate ranges that add up to 100 percent by weight.

	Weight Percent		
	Active Ingredient	Diluent	Surfactant
Water-Dispersible and Water-soluble Granules, Tablets and Powders.	5–90	0–94	1–15
Suspensions, Emulsions, Solutions (including Emulsifiable Concentrates)	5–50	40–95	0–15
Dusts	1–25	70–99	0–5
Granules and Pellets	0.01–99	5–99.99	0–15
High Strength Compositions	90–99	0–10	0–2

Typical solid diluents are described in Watkins, et al., *Handbook of Insecticide Dust Diluents and Carriers*, 2nd Ed., Dorland Books, Caldwell, New Jersey. Typical liquid diluents are described in Marsden, *Solvents Guide*, 2nd Ed., Interscience, New York, 1950. *McCutcheon's Detergents and Emulsifiers Annual*, Allured Publ. Corp., Ridgewood, New Jersey, as well as Sisely and Wood, *Encyclopedia of Surface Active Agents*, Chemical Publ. Co., Inc., New York, 1964, list surfactants and recommended uses. All formulations can contain minor amounts of additives to reduce foam, caking, corrosion, microbiological growth and the like, or thickeners to increase viscosity.

Surfactants include, for example, polyethoxylated alcohols, polyethoxylated alkylphenols, polyethoxylated sorbitan fatty acid esters, dialkyl sulfosuccinates, alkyl

sulfates, alkylbenzene sulfonates, organosilicones, *N,N*-dialkyltaurates, lignin sulfonates, naphthalene sulfonate formaldehyde condensates, polycarboxylates, and polyoxyethylene/polyoxypropylene block copolymers. Solid diluents include, for example, clays such as bentonite, montmorillonite, attapulgite and kaolin, starch, sugar, silica, talc, diatomaceous earth, urea, calcium carbonate, sodium carbonate and bicarbonate, and sodium sulfate. Liquid diluents include, for example, water, *N,N*-dimethylformamide, dimethyl sulfoxide, *N*-alkylpyrrolidone, ethylene glycol, polypropylene glycol, paraffins, alkylbenzenes, alkylnaphthalenes, oils of olive, castor, linseed, tung, sesame, corn, peanut, cotton-seed, soybean, rape-seed and coconut, fatty acid esters, ketones such as cyclohexanone, 2-heptanone, isophorone and 4-hydroxy-4-methyl-2-pentanone, and alcohols such as methanol, cyclohexanol, decanol and tetrahydrofurfuryl alcohol.

Solutions, including emulsifiable concentrates, can be prepared by simply mixing the ingredients. Dusts and powders can be prepared by blending and, usually, grinding as in a hammer mill or fluid-energy mill. Suspensions are usually prepared by wet-milling; see, for example, U.S. 3,060,084. Granules and pellets can be prepared by spraying the active material upon preformed granular carriers or by agglomeration techniques. See Browning, "Agglomeration", *Chemical Engineering*, December 4, 1967, pp 147–48, *Perry's Chemical Engineer's Handbook*, 4th Ed., McGraw-Hill, New York, 1963, pages 8–57 and following, and PCT Publication WO 91/13546. Pellets can be prepared as described in U.S. 4,172,714. Water-dispersible and water-soluble granules can be prepared as taught in U.S. 4,144,050, U.S. 3,920,442 and DE 3,246,493. Tablets can be prepared as taught in U.S. 5,180,587, U.S. 5,232,701 and U.S. 5,208,030. Films can be prepared as taught in GB 2,095,558 and U.S. 3,299,566.

For further information regarding the art of formulation, see T. S. Woods, "The Formulator's Toolbox – Product Forms for Modern Agriculture" in *Pesticide Chemistry and Bioscience, The Food–Environment Challenge*, T. Brooks and T. R. Roberts, Eds., Proceedings of the 9th International Congress on Pesticide Chemistry, The Royal Society of Chemistry, Cambridge, 1999, pp. 120–133. See also U.S. 3,235,361, Col. 6, line 16 through Col. 7, line 19 and Examples 10–41; U.S. 3,309,192, Col. 5, line 43 through Col. 7, line 62 and Examples 8, 12, 15, 39, 41, 52, 53, 58, 132, 138–140, 162–164, 166, 167 and 169–182; U.S. 2,891,855, Col. 3, line 66 through Col. 5, line 17 and Examples 1–4; Klingman, *Weed Control as a Science*, John Wiley and Sons, Inc., New York, 1961, pp 81–96; and Hance et al., *Weed Control Handbook*, 8th Ed., Blackwell Scientific Publications, Oxford, 1989.

In the following Examples, all percentages are by weight and all formulations are prepared in conventional ways. Compound numbers refer to compounds in Index Table A.

Example A

Wettable Powder

Compound 214	65.0%
dodecylphenol polyethylene glycol ether	2.0%
sodium ligninsulfonate	4.0%
sodium silicoaluminate	6.0%
montmorillonite (calcined)	23.0%.

Example B

Granule

Compound 214	10.0%
attapulgite granules (low volatile matter, 0.71/0.30 mm; U.S.S. No. 25–50 sieves)	90.0%.

Example C

Extruded Pellet

Compound 214	25.0%
anhydrous sodium sulfate	10.0%
crude calcium ligninsulfonate	5.0%
sodium alkylnaphthalenesulfonate	1.0%
calcium/magnesium bentonite	59.0%.

Example D

Emulsifiable Concentrate

Compound 214	20.0%
blend of oil soluble sulfonates and polyoxyethylene ethers	10.0%
isophorone	70.0%.

Example E

Granule

Compound 214	0.5%
cellulose	2.5%
lactose	4.0%
cornmeal	93.0%.

Compounds of this invention are characterized by favorable metabolic and/or soil residual patterns and exhibit activity controlling a spectrum of agronomic and non-agronomic invertebrate pests. (In the context of this disclosure "invertebrate pest control" means inhibition of invertebrate pest development (including mortality) that causes significant reduction in feeding or other injury or damage caused by the pest; related

expressions are defined analogously.) As referred to in this disclosure, the term "invertebrate pest" includes arthropods, gastropods and nematodes of economic importance as pests. The term "arthropod" includes insects, mites, spiders, scorpions, centipedes, millipedes, pill bugs and symphylans. The term "gastropod" includes snails, slugs and other Stylommatophora. The term "nematode" includes all of the helminths, such as: roundworms, heartworms, and phytophagous nematodes (Nematoda), flukes (Tematoda), Acanthocephala, and tapeworms (Cestoda). Those skilled in the art will recognize that not all compounds are equally effective against all pests. Compounds of this invention display activity against economically important agronomic, forest, greenhouse, nursery, ornamentals, food and fiber, public and animal health, domestic and commercial structure, household, and stored product pests. These include larvae of the order Lepidoptera, such as armyworms, cutworms, loopers, and heliothines in the family Noctuidae (e.g., fall armyworm (*Spodoptera fugiperda* J. E. Smith), beet armyworm (*Spodoptera exigua* Hübner), black cutworm (*Agrotis ipsilon* Hufnagel), cabbage looper (*Trichoplusia ni* Hübner), tobacco budworm (*Heliothis virescens* Fabricius)); borers, casebearers, webworms, coneworms, cabbageworms and skeletonizers from the family Pyralidae (e.g., European corn borer (*Ostrinia nubilalis* Hübner), navel orangeworm (*Amyelois transitella* Walker), corn root webworm (*Crambus caliginosellus* Clemens), sod webworm (*Herpetogramma licarsisalis* Walker)); leafrollers, budworms, seed worms, and fruit worms in the family Tortricidae (e.g., codling moth (*Cydia pomonella* Linnaeus), grape berry moth (*Endopiza viteana* Clemens), oriental fruit moth (*Grapholita molesta* Busck)); and many other economically important lepidoptera (e.g., diamondback moth (*Plutella xylostella* Linnaeus), pink bollworm (*Pectinophora gossypiella* Saunders), gypsy moth (*Lymantria dispar* Linnaeus)); nymphs and adults of the order Blattodea including cockroaches from the families Blattellidae and Blattidae (e.g., oriental cockroach (*Blatta orientalis* Linnaeus), Asian cockroach (*Blatella asahinai* Mizukubo), German cockroach (*Blattella germanica* Linnaeus), brownbanded cockroach (*Supella longipalpa* Fabricius), American cockroach (*Periplaneta americana* Linnaeus), brown cockroach (*Periplaneta brunnea* Burmeister), Madeira cockroach (*Leucophaea maderae* Fabricius)); foliar feeding larvae and adults of the order Coleoptera including weevils from the families Anthribidae, Bruchidae, and Curculionidae (e.g., boll weevil (*Anthonomus grandis* Boheman), rice water weevil (*Lissorhoptrus oryzophilus* Kuschel), granary weevil (*Sitophilus granarius* Linnaeus), rice weevil (*Sitophilus oryzae* Linnaeus)); flea beetles, cucumber beetles, rootworms, leaf beetles, potato beetles, and leafminers in the family Chrysomelidae (e.g., Colorado potato beetle (*Leptinotarsa decemlineata* Say), western corn rootworm (*Diabrotica virgifera virgifera* LeConte)); chafers and other beetles from the family Scaribaeidae (e.g., Japanese beetle (*Popillia japonica* Newman) and European chafer (*Rhizotrogus majalis* Razoumowsky)); carpet beetles from the family Dermestidae; wireworms from the family

Elateridae; bark beetles from the family Scolytidae and flour beetles from the family Tenebrionidae. In addition it includes: adults and larvae of the order Dermaptera including earwigs from the family Forficulidae (e.g., European earwig (*Forficula auricularia* Linnaeus), black earwig (*Chelisoches morio* Fabricius)); adults and nymphs of the orders Hemiptera and Homoptera such as, plant bugs from the family Miridae, cicadas from the family Cicadidae, leafhoppers (e.g. *Empoasca* spp.) from the family Cicadellidae, planthoppers from the families Fulgoroidae and Delphacidae, treehoppers from the family Membracidae, psyllids from the family Psyllidae, whiteflies from the family Aleyrodidae, aphids from the family Aphididae, phylloxera from the family Phylloxeridae, mealybugs from the family Pseudococcidae, scales from the families Coccidae, Diaspididae and Margarodidae, lace bugs from the family Tingidae, stink bugs from the family Pentatomidae, cinch bugs (e.g., *Blissus* spp.) and other seed bugs from the family Lygaeidae, spittlebugs from the family Cercopidae squash bugs from the family Coreidae, and red bugs and cotton stainers from the family Pyrrhocoridae. Also included are adults and larvae of the order Acari (mites) such as spider mites and red mites in the family Tetranychidae (e.g., European red mite (*Panonychus ulmi* Koch), two spotted spider mite (*Tetranychus urticae* Koch), McDaniel mite (*Tetranychus mcdanieli* McGregor)), flat mites in the family Tenuipalpidae (e.g., citrus flat mite (*Brevipalpus lewisi* McGregor)), rust and bud mites in the family Eriophyidae and other foliar feeding mites and mites important in human and animal health, i.e. dust mites in the family Epidermoptidae, follicle mites in the family Demodicidae, grain mites in the family Glycyphagidae, ticks in the order Ixodidae (e.g., deer tick (*Ixodes scapularis* Say), Australian paralysis tick (*Ixodes holocyclus* Neumann), American dog tick (*Dermacentor variabilis* Say), lone star tick (*Amblyomma americanum* Linnaeus) and scab and itch mites in the families Psoroptidae, Pyemotidae, and Sarcoptidae; adults and immatures of the order Orthoptera including grasshoppers, locusts and crickets (e.g., migratory grasshoppers (e.g., *Melanoplus sanguinipes* Fabricius, *M. differentialis* Thomas), American grasshoppers (e.g., *Schistocerca americana* Drury), desert locust (*Schistocerca gregaria* Forskal), migratory locust (*Locusta migratoria* Linnaeus), house cricket (*Acheta domesticus* Linnaeus), mole crickets (*Gryllotalpa* spp.)); adults and immatures of the order Diptera including leafminers, midges, fruit flies (Tephritidae), frit flies (e.g., *Oscinella frit* Linnaeus), soil maggots, house flies (e.g., *Musca domestica* Linnaeus), lesser house flies (e.g., *Fannia canicularis* Linnaeus, *F. femoralis* Stein), stable flies (e.g., *Stomoxys calcitrans* Linnaeus), face flies, horn flies, blow flies (e.g., *Chrysomya* spp., *Phormia* spp.), and other muscoid fly pests, horse flies (e.g., *Tabanus* spp.), bot flies (e.g., *Gastrophilus* spp., *Oestrus* spp.), cattle grubs (e.g., *Hypoderma* spp.), deer flies (e.g., *Chrysops* spp.), keds (e.g., *Melophagus ovinus* Linnaeus) and other Brachycera, mosquitoes (e.g., *Aedes* spp., *Anopheles* spp., *Culex* spp.), black flies (e.g., *Prosimulium* spp., *Simulium* spp.), biting midges, sand flies, sciarids, and other Nematocera; adults and immatures of the order

Thysanoptera including onion thrips (*Thrips tabaci* Lindeman) and other foliar feeding thrips; insect pests of the order Hymenoptera including ants (e.g., red carpenter ant (*Camponotus ferrugineus* Fabricius), black carpenter ant (*Camponotus pennsylvanicus* De Geer), Pharaoh ant (*Monomorium pharaonis* Linnaeus), little fire ant (*Wasmannia auropunctata* Roger), fire ant (*Solenopsis geminata* Fabricius), red imported fire ant (*Solenopsis invicta* Buren), Argentine ant (*Iridomyrmex humilis* Mayr), crazy ant (*Paratrechina longicornis* Latreille), pavement ant (*Tetramorium caespitum* Linnaeus), cornfield ant (*Lasius alienus* Förster), odorous house ant (*Tapinoma sessile* Say)), bees (including carpenter bees), hornets, yellow jackets and wasps; insect pests of the order Isoptera including the eastern subterranean termite (*Reticulitermes flavipes* Kollar), western subterranean termite (*Reticulitermes hesperus* Banks), Formosan subterranean termite (*Coptotermes formosanus* Shiraki), West Indian drywood termite (*Incisitermes immigrans* Snyder) and other termites of economic importance; insect pests of the order Thysanura such as silverfish (*Lepisma saccharina* Linnaeus) and firebrat (*Thermobia domestica* Packard); insect pests of the order Mallophaga and including the head louse (*Pediculus humanus capitis* De Geer), body louse (*Pediculus humanus humanus* Linnaeus), chicken body louse (*Menacanthus stramineus* Nitszch), dog biting louse (*Trichodectes canis* De Geer), fluff louse (*Goniocotes gallinae* De Geer), sheep body louse (*Bovicola ovis* Schrank), short-nosed cattle louse (*Haematopinus eurysternus* Nitzsch), long-nosed cattle louse (*Linognathus vituli* Linnaeus) and other sucking and chewing parasitic lice that attack man and animals; insect pests of the order Siphonoptera including the oriental rat flea (*Xenopsylla cheopis* Rothschild), cat flea (*Ctenocephalides felis* Bouche), dog flea (*Ctenocephalides canis* Curtis), hen flea (*Ceratophyllus gallinae* Schrank), sticktight flea (*Echidnophaga gallinacea* Westwood), human flea (*Pulex irritans* Linnaeus) and other fleas afflicting mammals and birds. Additional arthropod pests covered include: spiders in the order Araneae such as the brown recluse spider (*Loxosceles reclusa* Gertsch & Mulaik) and the black widow spider (*Latrodectus mactans* Fabricius), and centipedes in the order Scutigeromorpha such as the house centipede (*Scutigera coleoptrata* Linnaeus). Activity also includes members of the Classes Nematoda, Cestoda, Trematoda, and Acanthocephala including economically important members of the orders Strongylida, Ascaridida, Oxyurida, Rhabditida, Spirurida, and Enoplida such as but not limited to economically important agricultural pests (i.e. root knot nematodes in the genus *Meloidogyne*, lesion nematodes in the genus *Pratylenchus*, stubby root nematodes in the genus *Trichodorus*, etc.) and animal and human health pests (i.e. all economically important flukes, tapeworms, and roundworms, such as *Strongylus vulgaris* in horses, *Toxocara canis* in dogs, *Haemonchus contortus* in sheep, *Dirofilaria immitis* Leidy in dogs, *Anoplocephala perfoliata* in horses, *Fasciola hepatica* Linnaeus in ruminants, etc.).

Compounds of the invention show particularly high activity against pests in the order Lepidoptera (e.g., *Alabama argillacea* Hübner (cotton leaf worm), *Archips argyrospila* Walker (fruit tree leaf roller), *A. rosana* Linnaeus (European leaf roller) and other *Archips* species, *Chilo suppressalis* Walker (rice stem borer), *Cnaphalocrosis medinalis* Guenee (rice leaf roller), *Crambus caliginosellus* Clemens (corn root webworm), *Crambus teterrellus* Zincken (bluegrass webworm), *Cydia pomonella* Linnaeus (codling moth), *Earias insulana* Boisduval (spiny bollworm), *Earias vittella* Fabricius (spotted bollworm), *Helicoverpa armigera* Hübner (American bollworm), *Helicoverpa zea* Boddie (corn earworm), *Heliothis virescens* Fabricius (tobacco budworm), *Herpetogramma licarsisalis* Walker (sod webworm), *Lobesia botrana* Denis & Schiffermüller (grape berry moth), *Pectinophora gossypiella* Saunders (pink bollworm), *Phyllocnistis citrella* Stainton (citrus leafminer), *Pieris brassicae* Linnaeus (large white butterfly), *Pieris rapae* Linnaeus (small white butterfly), *Plutella xylostella* Linnaeus (diamondback moth), *Spodoptera exigua* Hübner (beet armyworm), *Spodoptera litura* Fabricius (tobacco cutworm, cluster caterpillar), *Spodoptera frugiperda* J. E. Smith (fall armyworm), *Trichoplusia ni* Hübner (cabbage looper) and *Tuta absoluta* Meyrick (tomato leafminer)). Compounds of the invention also have commercially significant activity on members from the order Homoptera including: *Acyrthisiphon pisum* Harris (pea aphid), *Aphis craccivora* Koch (cowpea aphid), *Aphis fabae* Scopoli (black bean aphid), *Aphis gossypii* Glover (cotton aphid, melon aphid), *Aphis pomi* De Geer (apple aphid), *Aphis spiraecola* Patch (spirea aphid), *Aulacorthum solani* Kaltenbach (foxglove aphid), *Chaetosiphon fragaefolii* Cockerell (strawberry aphid), *Diuraphis noxia* Kurdjumov/Mordvilko (Russian wheat aphid), *Dysaphis plantaginea* Paaserini (rosy apple aphid), *Eriosoma lanigerum* Hausmann (woolly apple aphid), *Hyalopterus pruni* Geoffroy (mealy plum aphid), *Lipaphis erysimi* Kaltenbach (turnip aphid), *Metopolophium dirrhodum* Walker (cereal aphid), *Macrosipum euphorbiae* Thomas (potato aphid), *Myzus persicae* Sulzer (peach-potato aphid, green peach aphid), *Nasonovia ribisnigri* Mosley (lettuce aphid), *Pemphigus* spp. (root aphids and gall aphids), *Rhopalosiphum maidis* Fitch (corn leaf aphid), *Rhopalosiphum padi* Linnaeus (bird cherry-oat aphid), *Schizaphis graminum* Rondani (greenbug), *Sitobion avenae* Fabricius (English grain aphid), *Therioaphis maculata* Buckton (spotted alfalfa aphid), *Toxoptera aurantii* Boyer de Fonscolombe (black citrus aphid), and *Toxoptera citricida* Kirkaldy (brown citrus aphid); *Adelges* spp. (adelgids); *Phylloxera devastatrix* Pergande (pecan phylloxera); *Bemisia tabaci* Gennadius (tobacco whitefly, sweetpotato whitefly), *Bemisia argentifolii* Bellows & Perring (silverleaf whitefly), *Dialeurodes citri* Ashmead (citrus whitefly) and *Trialeurodes vaporariorum* Westwood (greenhouse whitefly); *Empoasca fabae* Harris (potato leafhopper), *Laodelphax striatellus* Fallen (smaller brown planthopper), *Macrolestes quadrilineatus* Forbes (aster leafhopper), *Nephotettix cinticeps* Uhler (green leafhopper), *Nephotettix nigropictus* Stål (rice leafhopper), *Nilaparvata lugens* Stål (brown planthopper),

Peregrinus maidis Ashmead (corn planthopper), *Sogatella furcifera* Horvath (white-backed planthopper), *Sogatodes orizicola* Muir (rice delphacid), *Typhlocyba pomaria* McAtee white apple leafhopper, *Erythroneoura* spp. (grape leafhoppers); *Magicidada septendecim* Linnaeus (periodical cicada); *Icerya purchasi* Maskell (cottony cushion scale), *Quadraspidiotus perniciosus* Comstock (San Jose scale); *Planococcus citri* Risso (citrus mealybug); *Pseudococcus* spp. (other mealybug complex); *Cacopsylla pyricola* Foerster (pear psylla), *Trioza diospyri* Ashmead (persimmon psylla). These compounds also have activity on members from the order Hemiptera including: *Acrosternum hilare* Say (green stink bug), *Anasa tristis* De Geer (squash bug), *Blissus leucopterus leucopterus* Say (chinch bug), *Corythuca gossypii* Fabricius (cotton lace bug), *Cyrtopeltis modesta* Distant (tomato bug), *Dysdercus suturellus* Herrich-Schäffer (cotton stainer), *Euchistus servus* Say (brown stink bug), *Euchistus variolarius* Palisot de Beauvois (one-spotted stink bug), *Graptosthetus* spp. (complex of seed bugs), *Leptoglossus corculus* Say (leaf-footed pine seed bug), *Lygus lineolaris* Palisot de Beauvois (tarnished plant bug), *Nezara viridula* Linnaeus (southern green stink bug), *Oebalus pugnax* Fabricius (rice stink bug), *Oncopeltus fasciatus* Dallas (large milkweed bug), *Pseudatomoscelis seriatus* Reuter (cotton fleahopper). Other insect orders controlled by compounds of the invention include Thysanoptera (e.g., *Frankliniella occidentalis* Pergande (western flower thrip), *Scirthothrips citri* Moulton (citrus thrip), *Sericothrips variabilis* Beach (soybean thrip), and *Thrips tabaci* Lindeman (onion thrip); and the order Coleoptera (e.g., *Leptinotarsa decemlineata* Say (Colorado potato beetle), *Epilachna varivestis* Mulsant (Mexican bean beetle) and wireworms of the genera *Agriotes*, *Athous* or *Limonius*).

Compounds of this invention can also be mixed with one or more other biologically active compounds or agents including insecticides, fungicides, nematocides, bactericides, acaricides, growth regulators such as rooting stimulants, chemosterilants, semiochemicals, repellents, attractants, pheromones, feeding stimulants, other biologically active compounds or entomopathogenic bacteria, virus or fungi to form a multi-component pesticide giving an even broader spectrum of agricultural utility. Thus compositions of the present invention can further comprise a biologically effective amount of at least one additional biologically active compound or agent. Examples of such biologically active compounds or agents with which compounds of this invention can be formulated are: insecticides such as abamectin, acephate, acetamiprid, amidoflumet (S-1955), avermectin, azadirachtin, azinphos-methyl, bifenthrin, binfenazate, buprofezin, carbofuran, chlorfenapyr, chlorfluazuron, chlorpyrifos, chlorpyrifos-methyl, chromafenozide, clothianidin, cyfluthrin, beta-cyfluthrin, cyhalothrin, lambda-cyhalothrin, cypermethrin, cyromazine, deltamethrin, diafenthiuron, diazinon, diflubenzuron, dimethoate, diofenolan, emamectin, endosulfan, esfenvalerate, ethiprole, fenothicarb, fenoxycarb, fenpropathrin, fenproximate, fenvalerate, fipronil, flonicamid, flucythrinate, tau-fluvalinate, flufenerim (UR-50701), flufenoxuron, fonophos, halofenozide,

hexaflumuron, imidacloprid, indoxacarb, isofenphos, lufenuron, malathion, metaldehyde, methamidophos, methidathion, methomyl, methoprene, methoxychlor, monocrotophos, methoxyfenozide, nithiazin, novaluron, noviflumuron (XDE-007), oxamyl, parathion, parathion-methyl, permethrin, phorate, phosalone, phosmet, phosphamidon, pirimicarb, profenofos, pymetrozine, pyridalyl, pyriproxyfen, rotenone, spinosad, spiromesifin (BSN 2060), sulprofos, tebufenozide, teflubenzuron, tefluthrin, terbufos, tetrachlorvinphos, thiacloprid, thiamethoxam, thiodicarb, thiosultap-sodium, tralomethrin, trichlorfon and triflumuron; fungicides such as acibenzolar, azoxystrobin, benomyl, blasticidin-S, Bordeaux mixture (tribasic copper sulfate), bromuconazole, carpropamid, captafol, captan, carbendazim, chloroneb, chlorothalonil, copper oxychloride, copper salts, cyflufenamid, cymoxanil, cyproconazole, cyprodinil, (*S*)-3,5-dichloro-*N*-(3-chloro-1-ethyl-1-methyl-2-oxopropyl)-4-methylbenzamide (RH 7281), diclocymet (S-2900), diclomezine, dicloran, difenoconazole, (*S*)-3,5-dihydro-5-methyl-2-(methylthio)-5-phenyl-3-(phenylamino)-4*H*-imidazol-4-one (RP 407213), dimethomorph, dimoxystrobin, diniconazole, diniconazole-M, dodine, edifenphos, epoxiconazole, famoxadone, fenamidone, fenarimol, fenbuconazole, fencaramid (SZX0722), fenpiclonil, fenpropidin, fenpropimorph, fentin acetate, fentin hydroxide, fluazinam, fludioxonil, flumetover (RPA 403397), flumorf/flumorlin (SYP-L190), fluoxastrobin (HEC 5725), fluquinconazole, flusilazole, flutolanil, flutriafol, folpet, fosetyl-aluminum, furalaxyl, furametapyr (S-82658), hexaconazole, ipconazole, iprobenfos, iprodione, isoprothiolane, kasugamycin, kresoxim-methyl, mancozeb, maneb, mefenoxam, mepronil, metalaxyl, metconazole, metominostrobin/fenominostrobin (SSF-126), metrafenone (AC 375839), myclobutanil, neo-asozin (ferric methanearsonate), nicobifen (BAS 510), orysastrobin, oxadixyl, penconazole, pencycuron, probenazole, prochloraz, propamocarb, propiconazole, proquinazid (DPX-KQ926), prothioconazole (JAU 6476), pyrifenox, pyraclostrobin, pyrimethanil, pyroquilon, quinoxyfen, spiroxamine, sulfur, tebuconazole, tetraconazole, thiabendazole, thifluzamide, thiophanate-methyl, thiram, tiadinil, triadimefon, triadimenol, tricyclazole, trifloxystrobin, triticonazole, validamycin and vinclozolin; nematocides such as aldicarb, oxamyl and fenamiphos; bactericides such as streptomycin; acaricides such as amitraz, chinomethionat, chlorobenzilate, cyhexatin, dicofol, dienochlor, etoxazole, fenazaquin, fenbutatin oxide, fenpropathrin, fenpyroximate, hexythiazox, propargite, pyridaben and tebufenpyrad; and biological agents such as *Bacillus thuringiensis* including ssp. *aizawai* and *kurstaki*, *Bacillus thuringiensis* delta endotoxin, baculovirus, and entomopathogenic bacteria, virus and fungi.

A general reference for these agricultural protectants is *The Pesticide Manual, 12th Edition*, C. D. S. Tomlin, Ed., British Crop Protection Council, Farnham, Surrey, U.K., 2000.

Preferred insecticides and acaricides for mixing with compounds of this invention include pyrethroids such as cypermethrin, cyhalothrin, cyfluthrin and beta-cyfluthrin,

esfenvalerate, fenvalerate and tralomethrin; carbamates such as fenothicarb, methomyl, oxamyl and thiodicarb; neonicotinoids such as clothianidin, imidacloprid and thiacloprid, neuronal sodium channel blockers such as indoxacarb, insecticidal macrocyclic lactones such as spinosad, abamectin, avermectin and emamectin; γ-aminobutyric acid (GABA) antagonists such as endosulfan, ethiprole and fipronil; insecticidal ureas such as flufenoxuron and triflumuron, juvenile hormone mimics such as diofenolan and pyriproxyfen; pymetrozine; and amitraz. Preferred biological agents for mixing with compounds of this invention include *Bacillus thuringiensis* and *Bacillus thuringiensis* delta endotoxin as well as naturally occurring and genetically modified viral insecticides including members of the family Baculoviridae as well as entomophagous fungi.

Most preferred mixtures include a mixture of a compound of this invention with cyhalothrin; a mixture of a compound of this invention with beta-cyfluthrin; a mixture of a compound of this invention with esfenvalerate; a mixture of a compound of this invention with methomyl; a mixture of a compound of this invention with imidacloprid; a mixture of a compound of this invention with thiacloprid; a mixture of a compound of this invention with indoxacarb; a mixture of a compound of this invention with abamectin; a mixture of a compound of this invention with endosulfan; a mixture of a compound of this invention with ethiprole; a mixture of a compound of this invention with fipronil; a mixture of a compound of this invention with flufenoxuron; a mixture of a compound of this invention with pyriproxyfen; a mixture of a compound of this invention with pymetrozine; a mixture of a compound of this invention with amitraz; a mixture of a compound of this invention with *Bacillus thuringiensis* and a mixture of a compound of this invention with *Bacillus thuringiensis* delta endotoxin.

In certain instances, combinations with other invertebrate pest control compounds or agents having a similar spectrum of control but a different mode of action will be particularly advantageous for resistance management. Thus, compositions of the present invention can further comprise an biologically effective amount of at least one additional invertebrate pest control compounds or agents having a similar spectrum of control but a different mode of action. Contacting a plant genetically modified to express a plant protection compound (e.g., protein) or the locus of the plant with a biologically effective amount of a compound of invention can also provide a broader spectrum of plant protection and be advantageous for resistance management.

Invertebrate pests are controlled and protection of agronomic, horticultural and specialty crops, animal and human health is achieved by applying one or more of the compounds of this invention, in an effective amount, to the environment of the pests including the agronomic and/or nonagronomic locus of infestation, to the area to be protected, or directly on the pests to be controlled. Thus, the present invention further comprises a method for the control of foliar- and soil-inhabiting invertebrates and protection

of agronomic and/or nonagronomic crops, comprising contacting the invertebrates or their environment with a biologically effective amount of one or more of the compounds of the invention, or with a composition comprising at least one such compound or a composition comprising at least one such compound and an effective amount of at least one additional biologically active compound or agent. A preferred method of contact is by spraying. Alternatively, a granular composition comprising a compound of the invention can be applied to the plant foliage or the soil. Compounds of this invention are effective in delivery through plant uptake by contacting the plant with a composition comprising a compound of this invention applied as a soil drench of a liquid formulation, a granular formulation to the soil, a nursery box treatment or a dip of transplants. Other methods of contact include application of a compound or a composition of the invention by direct and residual sprays, aerial sprays, seed coats, microencapsulations, systemic uptake, baits, eartags, boluses, foggers, fumigants, aerosols, dusts and many others.

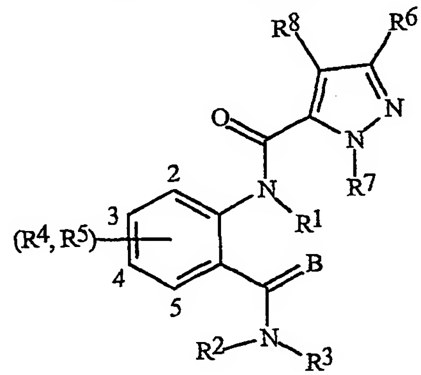
The compounds of this invention can be incorporated into baits that are consumed by the invertebrates or within devices such as traps and the like. Granules or baits comprising between 0.01–5% active ingredient, 0.05–10% moisture retaining agent(s) and 40–99% vegetable flour are effective in controlling soil insects at very low application rates, particularly at doses of active ingredient that are lethal by ingestion rather than by direct contact.

The compounds of this invention can be applied in their pure state, but most often application will be of a formulation comprising one or more compounds with suitable carriers, diluents, and surfactants and possibly in combination with a food depending on the contemplated end use. A preferred method of application involves spraying a water dispersion or refined oil solution of the compounds. Combinations with spray oils, spray oil concentrations, spreader stickers, adjuvants, other solvents, and synergists such as piperonyl butoxide often enhance compound efficacy.

The rate of application required for effective control (i.e. "biologically effective amount") will depend on such factors as the species of invertebrate to be controlled, the pest's life cycle, life stage, its size, location, time of year, host crop or animal, feeding behavior, mating behavior, ambient moisture, temperature, and the like. Under normal circumstances, application rates of about 0.01 to 2 kg of active ingredient per hectare are sufficient to control pests in agronomic ecosystems, but as little as 0.0001 kg/hectare may be sufficient or as much as 8 kg/hectare may be required. For nonagronomic applications, effective use rates will range from about 1.0 to 50 mg/square meter but as little as 0.1 mg/square meter may be sufficient or as much as 150 mg/square meter may be required. One skilled in the art can easily determine the biologically effective amount necessary for the desired level of invertebrate pest control.

The following Tests in the Biological Examples of the Invention demonstrate the efficacy of methods of the invention for protecting plants from specific arthropod pests. "Control efficacy" represents inhibition of arthropod development (including mortality) that causes significantly reduced feeding. The pest control protection afforded by the compounds is not limited, however, to these species. See Index Table A for compound descriptions. The following abbreviations are used in the Index Table which follows: *t* is tertiary, *n* is normal, *i* is iso, *s* is secondary, *c* is cyclo, Me is methyl, Et is ethyl, Pr is propyl and Bu is butyl; accordingly *i*-Pr is isopropyl, *s*-Bu is secondary butyl, etc. The abbreviation "Ex." stands for "Example" and is followed by a number indicating in which example the compound is prepared.

INDEX TABLE A



R^1, R^5, and R^8 are H, except where indicated; B is O, except where indicated. "CN" is bonded through carbon, not nitrogen; for example "CN-Ph" specifies cyanophenyl, not isocyanophenyl

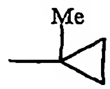
Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
1	*i*-Pr	H	2-Me	CF_3	CH_3	200–204
2 (Ex. 1)	*i*-Pr	H	2-Me	CF_3	Et	123–126
3	*i*-Pr	H	2-Cl	CF_3	CH_3	233–235
4	*t*-Bu	H	2-Me	CF_3	Et	215–218
5	*i*-Pr	H	2-Me	CH_3	Ph	238–239
6	*i*-Pr	H	2-Me	CH_3	CH_3	206–208
7	*i*-Pr	H	2-Me	CH_3	CH_2CF_3	246–248
8	*i*-Pr	H	2-Cl	Et	CF_3	235–237
9	*i*-Pr	H	2-Me	CH_3	CH_3, R^8 is Cl	205–207
10	*i*-Pr	H	2-Me	CH_3	4-CF_3-Ph	256–258
11	*i*-Pr	H	2-Me	CH_3	2-CF_3-Ph	204–206
12	*t*-Bu	H	2-Me	CH_3	Ph	236–238
13	*i*-Pr	H	2-F	CH_3	Ph	227–229
14	*i*-Pr	H	5-F	CH_3	Ph	209–211
15	*i*-Pr	H	2-Cl	CH_3	Ph	233–234

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
16	*i*-Pr	H	H	CH_3	Ph	215–217
17	*i*-Pr	H	2-NO_2	CH_3	Ph	236–237
18	*i*-Pr	H	2-Cl	CF_3	Ph	240–242
19 (Ex. 2)	*i*-Pr	H	2-Me	CF_3	Ph	260–262
20	*i*-Pr	H	2-I	CH_3	Ph	250–251
21	*i*-Pr	H	2-I	CH_3	2-CF_3-Ph	251–253
22	H	H	2-Me	CH_3	Ph	253–255
23	Et	Et	2-Me	CH_3	Ph	182–184
24	*t*-Bu	H	2-Cl	CF_3	Ph	232–234
25	*i*-Pr	H	2-I	CF_3	Ph	271–273
26	*t*-Bu	H	2-I	CF_3	Ph	249–250
27	*i*-Pr	H	2-Me	CH_3	*t*-Bu	210–211
28	*i*-Pr	H	2-Br	CF_3	Ph	257–259
29	*i*-Pr	H	2-Br	CH_3	Ph	246–247
30	*i*-Pr	H	2-Me	CF_3	2-pyridinyl	237–238
31	*i*-Pr	H	2,5-di-Cl	CF_3	Ph	>250
32	*i*-Pr, B is S	H	2-Me	CF_3	Ph	169–172
33	*i*-Pr	H	2-Me	CF_3	2-Cl-Ph	208–209
34	*i*-Pr	H	2-Cl	CF_3	2-Cl-Ph	234–235
35	*i*-Pr	H	2-Me	CF_3	4-Cl-Ph	289–290
36	*i*-Pr	H	2-Cl	CF_3	4-Cl-Ph	276–278
37	*i*-Pr	H	2-Cl	CF_3	2-pyridinyl	239–240
38	*i*-Pr	H	2-Me	CF_3	2-pyrimidinyl	205–208
39	*i*-Pr	H	2-Me	CF_3	2-(3-CH_3-pyridinyl)	183–187
40	*i*-Pr	H	2-Me	CF_2CF_3	Ph	231–232
41	*i*-Pr	H	2-Cl	CF_2CF_3	Ph	206–207
42	*t*-Bu	H	2-Cl	CF_2CF_3	Ph	212–213
43	*i*-Pr	H	2-Br	CF_2CF_3	Ph	219–222
44	*i*-Pr	H	2-Me	CF_3	3-Cl-Ph	278–280
45	*i*-Pr	H	2-Cl	CF_3	3-Cl-Ph	272–273
46	*i*-Pr	H	2-Me	CF_3	2-F-Ph	217–218
47	*i*-Pr	H	2-Cl	CF_3	2-F-Ph	220–221
48	*i*-Pr	H	2-Me	CF_3	4-F-Ph	269–270
49	*i*-Pr	H	2-Cl	CF_3	4-F-Ph	279–280
52	*i*-Pr	H	2-CF_3	CF_3	Ph	247–249
53	*i*-Pr	H	2-Cl	CF_3	*i*-Pr	255–258
54	*i*-Pr	H	2-Me	CF_3	3-F-Ph	277–278

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
55	*i*-Pr	H	2-Cl	CF_3	3-F-Ph	256–257
56	*i*-Pr	H	2-Me	CF_3	2-CF_3-Ph	215–216
57	*i*-Pr	H	2-Cl	CF_3	2-CF_3-Ph	230–231
58	*i*-Pr	H	2-Me	CF_3	2-Br-Ph	207–208
59	*i*-Pr	H	2-Cl	CF_3	2-Br-Ph	239–240
60	*i*-Pr	H	2-OCH_3	CF_3	Ph	215–216
61	*i*-Pr	H	5-Cl	CF_3	2-(3-CH_3-pyridinyl)	224–225
62	*i*-Pr	H	5-Me	CF_3	2-(3-Cl-pyridinyl)	179–181
63	*s*-Bu	H	2-Cl	CF_3	Ph	>240
64	*c*-Pr	H	2-Cl	CF_3	Ph	>240
65	Et	H	2-Cl	CF_3	Ph	>240
66	*t*-Bu	H	2-CF_3	CF_3	Ph	230–233
67	Et	H	2-CF_3	CF_3	Ph	246–249
68	$CH(CH_3)CH_2SCH_3$	H	2-CF_3	CF_3	Ph	215–217
69	$CH(CH_3)CH_2OCH_3$	H	2-CF_3	CF_3	Ph	220–223
70	*i*-Pr	H	5-Cl	CF_3	2-(3-Cl-pyridinyl)	230–233
71	*i*-Pr	H	5-Me	CF_3	2-thiazolyl	201-203
72	*i*-Pr	H	5-Me	CF_3	2-pyrazinyl	252-253
73	*i*-Pr	H	5-Me	CF_3	4-pyridinyl	224-228
74	*i*-Pr	H	2-Me	CF_3	*i*-Pr	236–243
75	*i*-Pr	H	2-Me	CF_3	2-CH_3-Ph	211–212
76	*i*-Pr	H	2-Cl	CF_3	2-CH_3-Ph	232–234
77	*i*-Pr	H	2-Br	CF_3	2-Cl-Ph	247–248
78	*t*-Bu	H	2-Me	CF_3	2-Cl-Ph	216–217
79 (Ex. 3)	*i*-Pr	H	2-Me	CF_3	2-(3-CF_3-pyridinyl)	227–230
80	CH_2CH_2Cl	H	2-Cl	CF_3	Ph	237–242
81	$CH_2CH_2CH_2Cl$	H	2-Cl	CF_3	Ph	233–239
82	$CH(CH_3)CO_2CH_3$	H	2-Cl	CF_3	Ph	221–222
83	$CH(i\text{-}Pr)CO_2CH_3$ (*S* configuration)	H	2-Cl	CF_3	Ph	212–213
84	*i*-Pr	H	2-Me	CF_3	2,6-di-Cl-Ph	267–268
85	*i*-Pr	H	2-Cl	CF_3	2,6-di-Cl-Ph	286–287
86	*i*-Pr	H	2-Me	Br	Ph	253–255
87	*i*-Pr	H	2-Cl	Br	Ph	247–248
88	*i*-Pr	H	2-Me	CF_3	*i*-Bu	205–210
89	*i*-Pr	H	2-Me	CF_3	CH_2Ph	235–237
90	*i*-Pr	H	2-Me	CF_3	2-(3-CH_3O-pyridinyl)	221–222

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
91	*i*-Pr	H	2-Me	CF_3	3-pyridinyl	260–261
92	*i*-Pr	H	2-Me	CF_3	4-quinolinyl	>260
93	*i*-Pr	H	2-Me	CN	2-(3-Cl-pyridinyl)	203–204
94	*i*-Pr	H	2-Me	CF_3	2,4-di-F-Ph	245–246
95	*i*-Pr	H	2-Cl	CF_3	2,4-di-F-Ph	252–253
96	*i*-Pr	H	2-Me	CF_3	2-Et-Ph	207–209
97	*i*-Pr	H	2-Cl	CF_3	2-Et-Ph	221–222
98	*i*-Pr	H	H	CF_3	2-Cl-Ph	206–207
99	*t*-Bu	H	H	CF_3	2-Cl-Ph	197–198
100	$CH(CH_3)CH_2OCH_3$	H	H	CF_3	2-Cl-Ph	145–148
101	$CH(CH_3)CH_2SCH_3$	H	H	CF_3	2-Cl-Ph	158–160
102	$CH(CH_3)CH_2SCH_3$	H	2-Cl	CF_3	Ph	184–186
103	$CH(CH_3)CH_2OCH_3$	H	2-Cl	CF_3	Ph	217–218
104	*n*-Pr	H	2-Cl	CF_3	Ph	247–248
105	*i*-Bu	H	2-Cl	CF_3	Ph	244–245
106	CH_3	H	2-Cl	CF_3	Ph	>250
107	*i*-Pr	Me	2-Cl	CF_3	Ph	193–194
108	$CH_2C{\equiv}CH$	H	2-Cl	CF_3	Ph	>250
109	$CH_2CH{=}CH_2$	H	2-Cl	CF_3	Ph	248–249
110	CH_2(2-furanyl)	H	2-Cl	CF_3	Ph	246–247
113	*i*-Pr	H	2-Me	CF_3	4-(3,5-di-Cl-pyridinyl)	239–242
114	*i*-Pr	H	2-Cl	CF_3	4-(3,5-di-Cl-pyridinyl)	229–231
115	$CH(CH_3)CH_2SCH_3$	H	2-Me	CF_3	2-Cl-Ph	194–195
116	$CH(CH_3)CH_2OCH_3$	H	2-Me	CF_3	2-Cl-Ph	181–183
117	*s*-Bu	H	2-Me	CF_3	2-Cl-Ph	199–200
118	*c*-Pr	H	2-Me	CF_3	2-Cl-Ph	234–235
119	*n*-Pr	H	2-Me	CF_3	2-Cl-Ph	222–223
120	*i*-Bu	H	2-Me	CF_3	2-Cl-Ph	235–237
121	Me	H	2-Me	CF_3	2-Cl-Ph	242–243
122	*i*-Pr	Me	2-Me	CF_3	2-Cl-Ph	90–93
123	$CH_2C{\equiv}CH$	H	2-Me	CF_3	2-Cl-Ph	215–216
124	Et	H	2-Me	CF_3	2-Cl-Ph	228–229
125	$CH_2CH{=}CH_2$	H	2-Me	CF_3	2-Cl-Ph	227–228
126	CH_2(2-furanyl)	H	2-Me	CF_3	2-Cl-Ph	218–219
127	$CH(CH_3)CH_2SCH_3$	H	2-Me	CF_3	Ph	179–180
128	$CH(CH_3)CH_2OCH_3$	H	2-Me	CF_3	Ph	219–220
129	*s*-Bu	H	2-Me	CF_3	Ph	244–245

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
130	*c*-Pr	H	2-Me	CF_3	Ph	>250
131	*n*-Pr	H	2-Me	CF_3	Ph	238–239
132	*i*-Bu	H	2-Me	CF_3	Ph	237–238
133	Me	H	2-Me	CF_3	Ph	263–265
134	*i*-Pr	Me	2-Me	CF_3	Ph	178–179
135	$CH_2C{\equiv}CH$	H	2-Me	CF_3	Ph	253–254
136	Et	H	2-Me	CF_3	Ph	244–245
137	$CH_2CH{=}CH_2$	H	2-Me	CF_3	Ph	240–241
138	CH_2(2-furanyl)	H	2-Me	CF_3	Ph	245–246
139	*i*-Pr	H	2-$OCHF_2$	CF_3	2-Cl-Ph	200–201
140	*i*-Pr	H	2-OCH_3	CF_3	2-Cl-Ph	206–207
141	*i*-Pr	H	2-I	CF_3	2-Cl-Ph	253–256
142	*i*-Pr	H	2-Me	Br	2-Cl-Ph	147–150
143	*i*-Pr	H	2-Cl	Br	2-Cl-Ph	246–247
144	*i*-Pr	H	2-Me	CF_3	2-CH_3O-Ph	218–219
145	*i*-Pr	H	2-Cl	CF_3	2-CH_3O-Ph	243–244
146	*i*-Pr	H	2-Me	CF_3	1-isoquinolinyl	252–253
147	$CH(CH_3)CH_2SCH_3$	H	2-Cl	CF_3	2-Cl-Ph	217–218
148	$CH(CH_3)CH_2OCH_3$	H	2-Cl	CF_3	2-Cl-Ph	207–208
149	*s*-Bu	H	2-Cl	CF_3	2-Cl-Ph	216–217
150	*c*-Pr	H	2-Cl	CF_3	2-Cl-Ph	261–262
151	*n*-Pr	H	2-Cl	CF_3	2-Cl-Ph	231–232
152	*i*-Bu	H	2-Cl	CF_3	2-Cl-Ph	255–256
153	Me	H	2-Cl	CF_3	2-Cl-Ph	233–235
154	*i*-Pr	Me	2-Cl	CF_3	2-Cl-Ph	127–128
155	$CH_2C{\equiv}CH$	H	2-Cl	CF_3	2-Cl-Ph	226–227
156	Et	H	2-Cl	CF_3	2-Cl-Ph	244–246
157	$CH_2CH{=}CH_2$	H	2-Cl	CF_3	2-Cl-Ph	235–236
158	CH_2(2-furanyl)	H	2-Cl	CF_3	2-Cl-Ph	207–208
160	*i*-Pr	H	$C{\equiv}CH$	CF_3	2-Cl-Ph	228–230
161	*i*-Pr	H	2-Cl	$C{\equiv}CH$	2-Cl-Ph	219–222
162	*i*-Pr	H	2-Me	H	H, R^8 is CH_3	220–223
163	*i*-Pr	H	2-Me	CH_3	Ph, R^8 is Cl	209–210
164	*i*-Pr, B is S	H	2-Cl	CF_3	Ph	169–174
165	*i*-Pr	H	2-Me	CF_3	2,6-di-F-Ph	223–225
166	*i*-Pr	H	2-Me	CF_3	2-Cl-6-F-Ph	203–206
167	*i*-Pr	H	2-Cl	CF_3	2-Cl-6-F-Ph	218–221

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
168	*i*-Pr	H	2-Me-4-Br	CF_3	2-F-Ph	232–233
169	*t*-Bu	H	2-Cl	CF_3	2-(3-Cl-pyridinyl)	250–251
170		H	2-Cl	CF_3	2-(3-Cl-pyridinyl)	>250
171	Et	Et	2-Cl	CF_3	2-Cl-Ph	252–253
172	Me	Me	2-Cl	CF_3	2-Cl-Ph	234–235
173	Et	Et	2-Me	CF_3	2-Cl-Ph	237–238
174	Me	Me	2-Me	CF_3	2-Cl-Ph	225–226
176	*i*-Pr	H	2-Cl	CF_3	2-pyrazinyl	242–243
177	*t*-Bu	H	2-Me-4-Br	CF_3	2-Cl-Ph	>260
178	$CH(CH_3)CH_2OCH_3$	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	176–177
179	$CH(CH_3)CH_2SCH_3$	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	196–197
180	$CH(CH_3)CH_2OCH_3$	H	2-Cl	CF_3	2-(3-Cl-pyridinyl)	197–198
181	$CH(CH_3)CH_2SCH_3$	H	2-Cl	CF_3	2-(3-Cl-pyridinyl)	202–203
182	*i*-Pr	H	2-Me	CF_3	2-I-Ph	221–222
183	*i*-Pr	H	2-Cl	CF_3	2-I-Ph	238–240
184	*i*-Pr	H	2-Me	CF_3	2-(HC≡C)-Ph	215–217
185	*i*-Pr	H	2-Cl	CF_3	2-(HC≡C)-Ph	244–246
186	*i*-Pr	H	2-Me	CF_3	2-Cl-4-F-Ph	203–205
187	*i*-Pr	H	2-Cl	CF_3	2-Cl-4-F-Ph	218–219
188	Et	Et	2-Me	CF_3	2-Cl-Ph	243–247
189	*i*-Pr	H	2-Me	CF_3	2,6-di-Me-Ph	259–260
190	*i*-Pr	H	2-Cl	CF_3	2,6-di-Me-Ph	268–269
191	*i*-Pr	H	2-Me	CF_3	2,6-di-Cl-4-CN-Ph	*
192	*i*-Pr	H	2-Me	CF_3	2-CN-Ph	225–235
193	*i*-Pr	H	2-Me	CF_3	2-(CF_3O)-Ph	214–215
194	*i*-Pr	H	2-Cl	CF_3	2-(CF_3O)-Ph	223–224
195	*i*-Pr	H	2-Me	CF_3	2-Br-4-F-Ph	202–203
196	*i*-Pr	H	2-Cl	CF_3	2-Br-4-F-Ph	222–223
197	*i*-Pr	H	2-Me	CF_3	2-(3-Me-pyrazinyl)	205–207
198	Me	H	2-Cl	CF_3	2-(3-Cl-pyridinyl)	215–220
199	$CH_2C{\equiv}CH$	H	2-Cl	CF_3	2-(3-Cl-pyridinyl)	197–198
200	Me	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	193–196
201	Et	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	204–206
202	$CH_2C{\equiv}CH$	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	177–178
203	*i*-Pr	H	2-Me	CF_3	4-(8-Cl-quinolinyl)	>250
204	*i*-Pr	H	2-Me	CF_3	4-(2-Me-quinolinyl)	>250

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
205	*i*-Pr	H	2-Cl	CF_3	4-(2-Me-quinolinyl)	>250
206	*i*-Pr	H	2-Me	CF_3	4-(7-Cl-quinolinyl)	>250
207	*i*-Pr	H	2,4-Br_2	CF_3	2-Cl-Ph	233–234
208	*i*-Pr	H	2-Br	Br	2-Cl-Ph	255–258
209	Me	H	2-Me	Br	2-Cl-Ph	236–237
210	*t*-Bu	H	2-Cl	Br	2-Cl-Ph	260–261
211	Et	H	2-Me	Br	2-Cl-Ph	254–255
212	*t*-Bu	H	2-Me	Br	2-Cl-Ph	259–260
213	*c*-Bu	H	2-Cl	CN	2-(3-Cl-pyridinyl)	177–180
214 (Ex. 4, 5)	*i*-Pr	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	237–239
215	*i*-Pr	H	2-Me	CF_3	4-(6-Cl-quinolinyl)	>250
216	Me	Me	2-Me	CF_3	4-(6-Cl-quinolinyl)	>250
218	*i*-Pr	H	2-Cl	CN	2-(3-Cl-pyridinyl)	195–200
219	*t*-Bu	H	2-Cl	CN	2-(3-Cl-pyridinyl)	>250
220	Et	H	2-Cl	CN	2-(3-Cl-pyridinyl)	200–205
221	*i*-Pr	H	2-Cl	CF_3	2-(3-Me-pyrazinyl)	225–230
222	*t*-Bu	H	2-Cl	CF_3	2-(3-Me-pyrazinyl)	235–240
223	Et	H	2-Cl	CF_3	2-(3-Me-pyrazinyl)	210–220
224	*i*-Pr	H	2-Me	CF_3	3-(2-Cl-pyridinyl)	*
225	*i*-Pr	H	2-Cl	CF_3	2,3-di-Cl-Ph	217–219
226	*t*-Bu	H	2-Cl	CF_3	2,3-di-Cl-Ph	254–256
227	*i*-Pr	H	2-Me	CF_3	2,3-di-Cl-Ph	208–209
228	*t*-Bu	H	2-Me	CF_3	2,3-di-Cl-Ph	232–233
229	*t*-Bu	H	2-Me-4-Br	Br	2-Cl-Ph	239–241
230	Me	H	2-Me-4-Br	Br	2-Cl-Ph	150–152
231	Et	H	2-Me-4-Br	Br	2-Cl-Ph	223–225
232	*i*-Pr	H	2-Me-4-Br	Br	2-Cl-Ph	197–198
233	Me	H	2-Me	CF_3	2-F-Ph	245–247
234	$CH_2C{\equiv}CH$	H	2-Me	CF_3	2-F-Ph	222–227
235	Me	Me	2-Cl	CF_3	2-Cl-Ph	234–236
236	$CH_2C{\equiv}CH$	H	2-Me-4-Br	Br	2-Cl-Ph	187–188
237	*i*-Pr	H	2-Cl	CF_3	2-(3-Me-pyridinyl)	224–225
238	*i*-Pr	H	2-Cl	CF_3	2-(3-Cl-pyridinyl)	230–233
239	*i*-Pr	H	2-Me	CF_3	2-pyrazinyl	252–253
240	*i*-Pr	H	2-Me	CF_3	2-thiazolyl	201–203
241	*i*-Pr	H	2-Me	CF_3	4-pyridinyl	224–228
242	*i*-Pr	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	249–250

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
243	*i*-Pr	H	2-Me	CF_3	Ph, R^8 is CH_3	246–248
244	Me	Me	2-Me	CF_3	2-Cl-Ph	234–235
245	*i*-Pr	H	2-Me	CF_3	$CH{=}CHCH_3$	225–228
246	*i*-Pr	H	2-Me	CF_3	2-Cl-6-Me-Ph	
247	*i*-Pr	H	2-Cl	CF_3	2-Cl-6-Me-Ph	
248	*i*-Pr	H	2-Cl	CF_3	4-CN-Ph	*
249	*i*-Pr	H	2-Cl	CF_3	2,6-di-Cl-4-CN-Ph	*
250	*i*-Pr	H	2-Cl	CF_3	2-Cl-4-CN-Ph	*
251	*i*-Pr	H	2-Cl	CN	Ph	*
252	*i*-Pr	H	2-Me	CF_3	4-CN-Ph	271–272
253	*i*-Pr	H	2-Me	CF_3	3-CN-Ph	263–264
254	*i*-Pr	H	2-Me	CF_3	2-Cl-4-CN-Ph	*
255	*i*-Pr	H	2-Me	CN	Ph	*
256	*i*-Pr	H	2-Cl	CF_3	3-CN-Ph	*
257	*i*-Pr	H	2-Me	CF_3	2-Me-4-F-Ph	204-206
258	*i*-Pr	H	2-Cl	CF_3	2-Me-4-F-Ph	212-213
259	*i*-Pr	H	2-Me	CF_3	2,4-di-Me-Ph	189–190
260	*t*-Bu	H	2-Me	CF_3	2,4-di-Me-Ph	197–198
261	*t*-Bu	H	2-Cl	CF_3	2,4-di-Me-Ph	234–235
262	*i*-Pr	H	2-Me	CF_3	*n*-Bu, R^8 is Cl	95–98
263	Me	H	2-Cl	CF_3	4-(7-Cl-quinolinyl)	>250
264	Et	H	2-Cl	CF_3	4-(7-Cl-quinolinyl)	>250
265	$CH_2CH{=}CH_2$	H	2-Cl	CF_3	4-(7-Cl-quinolinyl)	>250
266	*i*-Pr	H	2-Cl	CF_3	4-(8-Cl-quinolinyl)	>250
267	*i*-Pr	H	2-Me	CF_3	2-(3-CN-pyridinyl)	237–239
268	*i*-Pr	H	2-Me	CF_3	1-(6-Cl-isoquinolinyl)	>250
269	*t*-Bu	H	2-Me	CF_3	1-(6-Cl-isoquinolinyl)	227–229
270	Me	Me	2-Me	CF_3	1-(6-Cl-isoquinolinyl)	>250
271	*i*-Pr	H	2-Me	CF_3	2-Cl-4-CN-6-Me-Ph	*
272	*i*-Pr	H	2-Me-4-Br	Br	2-Cl-Ph	187–188
273	$CH_2CH(OCH_3)_2$	H	2-Me	CF_3	2-Cl-Ph	205–207
274	$CH_2CH(OCH_3)_2$	Me	2-Me	CF_3	2-Cl-Ph	185–190
275	$CH_2CH_2CH(OCH_3)_2$	H	2-Me	CF_3	2-Cl-Ph	85–90
276	Me	H	2-Me	CF_3	2,6-di-Cl-Ph	280-282
277	Et	H	2-Me	CF_3	2,6-di-Cl-Ph	274-275
278	*t*-Bu	H	2-Me	CF_3	2,6-di-Cl-Ph	285-286
279	*t*-Bu	H	2-Cl	CF_3	2,6-di-Cl-Ph	290-291

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
280	*i*-Pr	H	2-Me	H	2-Cl-Ph	*
281	*i*-Pr	H	2-Me	H	2-Me-Ph	*
282	*i*-Pr	H	2-Me	H	2-F-Ph	*
283	*i*-Pr	H	2-Me	Br	2-(3-Cl-pyridinyl)	206–209
284	CH_2CH_2CN	H	2-Me	CF_3	2-Cl-Ph	189–195
285	*i*-Pr	H	2-Me	CN	2-Cl-Ph	*
286	*i*-Pr	H	2-Me	CF_3	2-(3-CH_3O-pyrazinyl)	195–200
287	*i*-Pr	H	2-Me	Br	2,6-di-Cl-Ph	265-267
288	*t*-Bu	H	2-Me	Br	2,6-di-Cl-Ph	282-284
289	*i*-Pr	H	2-Cl	Br	2,6-di-Cl-Ph	277-279
290	*t*-Bu	H	2-Cl	Br	2,6-di-Cl-Ph	296-298
291	*i*-Pr	H	2-Me	Br	2-Cl-4-F-Ph	236-238
292	*t*-Bu	H	2-Me	Br	2-Cl-4-F-Ph	249-250
293	*i*-Pr	H	2-Cl	Br	2-Cl-4-F	176-177
294	*t*-Bu	H	2-Cl	Br	2-Cl-4-F-Ph	257-258
295	*i*-Pr	H	2-I	Br	2-Cl-4-F	227-229
296	*c*-Bu	H	2-Cl	CF_3	2-(3-Cl-pyridinyl)	230–231
297	*i*-Pr	H	2-Cl	Br	2-(3-Cl-pyridinyl)	231–234
298	*t*-Bu	H	2-Cl	Br	2-(3-Cl-pyridinyl)	245–248
299	Et	H	2-Cl	Br	2-(3-Cl-pyridinyl)	219–222
300	Et	H	2-Me	Br	2-(3-Cl-pyridinyl)	217–220
301	*t*-Bu	H	2-Me	Br	2-(3-Cl-pyridinyl)	237–240
302	CH_2CN	H	2-Me	Br	2-(3-Cl-pyridinyl)	227–229
303	*t*-Bu	H	2-Me	CN	2-(3-Cl-pyridinyl)	215–225
304	*c*-Bu	H	2-Me	CN	2-(3-Cl-pyridinyl)	105–115
305	*c*-Bu	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	187-190
306	*c*-pentyl	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	190–195
307	*s*-Bu	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	170–180
308	*c*-pentyl	H	2-Cl	CF_3	2-(3-Cl-pyridinyl)	215–222
309	*s*-Bu	H	2-Cl	CF_3	2-(3-Cl-pyridinyl)	210–220
313	*i*-Pr	H	2-Me	Cl	2-(3-Cl-pyridinyl)	204–206
314	*t*-Bu	H	2-Me	Cl	2-(3-Cl-pyridinyl)	210–213
315	*t*-Bu	H	2-Cl	Cl	2-(3-Cl-pyridinyl)	237–239
316	*i*-Pr	H	2-Cl	Cl	2-(3-Cl-pyridinyl)	159–162
317	$CH(CH_3)_2CH_2CH_3$	H	2-Me	CN	2-(3-Cl-pyridinyl)	165–175
318	*c*-hexyl	H	2-Cl	CF_3	2-(3-Cl-pyridinyl)	250–260
319	$CH(CH_3)_2CH_2CH_3$	H	2-Cl	CF_3	2-(3-Cl-pyridinyl)	200–210

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
320	*i*-Pr	H	2,4-di-Me	CF_3	2-Cl-Ph	239–240
321	*i*-Pr	H	2-Me	CF_3	2-Cl-5-CN-Ph	*
322	*i*-Pr	H	2-Me	H	2-(3-Cl-pyridinyl)	111–115
323	*i*-Pr	H	2-Me	CF_3	2-CO_2Me-Ph	
324	*i*-Pr	H	2-Me-4-Br	CF_3	2,6-di-Cl-Ph	230–233
325	*t*-Bu	H	2-Me-4-Br	CF_3	2,6-di-Cl-Ph	>250
326	Me	H	2-Me-4-Br	CF_3	2,6-di-Cl-Ph	228–230
327	CH_2CN	H	2-Me-4-Br	CF_3	2,6-di-Cl-Ph	228–230
328	*i*-Pr	H	2,4-di-Cl	CF3	2-Cl-Ph	223–224
329	*i*-Pr	H	2-Me	CF_3	2-Cl-4-CF_3-6-Cl-Ph	206–207
330	*i*-Pr	H	2-Me	CF_3	5-(1,3-di-Me-4-Cl-pyrazolyl)	231-232
331	*i*-Pr	H	2-Me	CF_3	2-(4,6-di-Me-pyrimidinyl)	220–222
332	*i*-Pr	H	2-Cl	CF_3	2-(4,6-di-Me-pyrimidinyl)	152–154
333	*t*-Bu	H	2-Me	CF_3	2-(4,6-di-Me-pyrimidinyl)	124–127
334	*t*-Bu	H	2-Cl	CF_3	2-(4,6-di-Me-pyrimidinyl)	179–182
335	*i*-Pr	H	4-I	CF_3	2-Cl-Ph	218–219
336	*i*-Pr	H	2-Me-4-OCH_3	CF_3	2-(3-Cl-pyridinyl)	187–188
337	*i*-Pr	H	2-Me	CF_3	2-F-4-Cl-5-(*i*-PrO)-Ph	214–216
338	CH_2CN	H	2-Me	Cl	2-(3-Cl-pyridinyl)	190–195
339	Et	H	2-Cl	CF_3	2-(3-Cl-pyridinyl)	217–219
340	*i*-Pr	H	2-Me-4-Br	CF_3	2,3-di-Cl-Ph	>250
341	*i*-Pr	H	2-Me	CF_3	2,5-di-Cl-Ph	>250
342	*i*-Pr	H	2-Cl-4-Br	CF_3	2,3-di-Cl-Ph	251–253
343	CH_2CN	H	2-Cl	CF_3	2,3-di-Cl-Ph	185–190
344	$CH_2CH_2SCH_2CH_3$	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	197–200
345	$CH_2CH_2CH_2SCH_3$	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	185–190
346	CH_2(2-furanyl)	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	210–215
347	$CH_2C(=CH_2)CH_3$	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	225–229
348	$CH_2CH_2OCH_3$	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	215–218
349	$CH_2CH_2CH_2OH$	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	210–212
350	CH_2CH_2Cl	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	206–216
351	CH_2CH_2OH	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	217–220
352	$CH(CH_3)CH_2OH$	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	110–115
353	$CH_2CH(Br)CH_2Br$	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	217–220
354	$CH_2CO_2CH_3$	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	>250
355	$CH_2CH(OH)CH_2OH$	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	>250

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
356	$CH_2CH_2CH_2Cl$	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	207–212
357	$CH(CH_2OH)CH_2CH_3$	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	173–176
358	*i*-Pr	H	2-Me	CF_3	2-(5-CF_3-pyridinyl)	270–275
359	Et	H	2-Me	CF_3	2-(3,6-di-Me-pyrazinyl)	210–215
360	*i*-Pr	H	2-Me	CF_3	2-(3,6-di-Me-pyrazinyl)	215–220
361	*t*-Bu	H	2-Me	CF_3	2-(3,6-di-Me-pyrazinyl)	265–270
362	Et	H	2-Cl	CF_3	2-(3,6-di-Me-pyrazinyl)	214–217
363	*i*-Pr	H	2-Cl	CF_3	2-(3,6-di-Me-pyrazinyl)	215–218
364	*i*-Pr	H	2-Me	OCH_3	2-Cl-Ph	137-140
365	*i*-Pr	H	2-Cl	OCH_3	2-Cl-Ph	155-158
366	*i*-Pr	H	2-Me	Me	2-Cl-Ph	151-154
367	*i*-Pr	H	2-Cl	Me	2,6-di-Cl-Ph	242-244
368	$CH_2CH(OH)CH_3$	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	123–125
369	$CH_2CH(OH)CH_2CH_3$	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	175–180
370	CH_2CN	H	2,4-di-Br	CF_3	2-(3-Cl-pyridinyl)	142–143
371	*c*-Pr	H	2,4-di-Br	CF_3	2-(3-Cl-pyridinyl)	213–214
372	CH_2CN	H	2,4-di-Cl	CF_3	2-(3-Cl-pyridinyl)	201–202
373	*i*-Pr	H	2,6-di-Me	CF_3	2-(3-Cl-pyridinyl)	204–205
374	*t*-Bu	H	2,6-di-Me	CF_3	2-(3-Cl-pyridinyl)	242–243
375	*t*-Bu	H	2-Me	CF_3	2-(5-CF_3-pyridinyl)	220–230
376	$C(CH_3)_2CH_2OH$	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	205–210
377	CH_2CH_2F	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	127–130
378	*i*-Pr	H	2-Me	CF_3	2-(4-Me-pyrimidinyl)	196–197
379	*i*-Pr	H	2-Cl	CF_3	2-(4-Me-pyrimidinyl)	208–210
380	*t*-Bu	H	2-Me	CF_3	2-(4-Me-pyrimidinyl)	180–182
381	*t*-Bu	H	2-Cl	CF_3	2-(4-Me-pyrimidinyl)	182–184
382	*s*-Bu	H	2-Me	CF_3	2-(3-Et-pyrazinyl)	160–165
383	Et	H	2-Me	CF_3	2-(3-Et-pyrazinyl)	185–190
384	*i*-Pr	H	2-Me	CF_3	2-(3-Et-pyrazinyl)	180–183
385	$CH_2CF_2CF_3$	H	2-Cl	CF_3	2-Cl-Ph	258–260
386	*t*-Bu	H	2-Me	CF_3	2-(3-Et-pyrazinyl)	180–185
387	CH_2CF_3	H	2-Cl	CF_3	2-Cl-Ph	262–264
388	CH_2CN	H	2-Me-4-Br	CF_3	2-(3-Cl-pyridinyl)	192–193
389	$CH(CH_3)CH_2OH$	H	2-Me	CF3	2-Cl-Ph	203-205
390	*i*-Pr	H	2-Me	Cl	2-Cl-Ph	207-209
391	*i*-Pr	H	2-Cl	Cl	2-Cl-Ph	236-237
392	*i*-Pr	H	2-Me	I	2-Cl-Ph	225-226

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
393	*i*-Pr	H	2-Cl	I	2-Cl-Ph	251-253
394	$CH(CH_3)CH_2Cl$	H	2-Me	CF_3	2-Cl-Ph	212–214
395	H	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	217–220
396	*i*-Pr	H	2-Cl	CF_3	4-(5,6-di-Me-pyrimidinyl)	218-220
397	*t*-Bu	H	2-Cl	CF_3	4-(5,6-di-Me-pyrimidinyl)	212–214
398	*i*-Pr	H	2-Cl	CF_3	4-(2,5,6-tri-Me-pyrimidinyl)	162–164
399	*i*-Pr	H	2-Me	CF_3	4-(5,6-di-Me-pyrimidinyl)	162–164
400	$CH_2CH(OH)CH_3$	H	2-Me	CF_3	2-Cl-Ph	207–209
401	H	H	2-Me	CF_3	2-Cl-Ph	230–232
402	$CH_2CH(Cl)CH_3$	H	2-Me	CF_3	2-Cl-Ph	230–232
403	CH_2CH_2CN	H	2-Cl	CF_3	2-(3-Cl-pyridinyl)	215–217
404	CH_2CH_2F	H	2-Cl	CF_3	2-(3-Cl-pyridinyl)	212–214
405	CH_2CH_2CN	H	2-Cl	CF_3	2-Cl-Ph	*
406	*i*-Pr	H	2-Me-4-Br	CN	2-(3-Cl-pyridinyl)	*
407	CH_2CN	H	2-Me-4-CF_3	CF_3	2-(3-Cl-pyridinyl)	211–213
408	*i*-Pr	H	2-Me	CF3	2,5-di-F-Ph	179–181
409	*i*-Pr	H	2,4-di-Br	CN	2-(3-Cl-pyridinyl)	*
410	*t*-Bu	H	2,4-di-Br	CN	2-(3-Cl-pyridinyl)	145–147
411	Me	H	2,4-di-Br	CN	2-(3-Cl-pyridinyl)	165–168
412	Et	H	2,4-di-Br	CN	2-(3-Cl-pyridinyl)	179–181
413	Me	H	2-Me-4-Br	Me	2-(3-Cl-pyridinyl)	141–143
414	*t*-Bu	H	2-Me-4-Br	Me	2-(3-Cl-pyridinyl)	161–163
415	*i*-Pr	H	2-Me-4-Br	Me	2-(3-Cl-pyridinyl)	141–143
416	Et	H	2-Me-4-Br	Me	2-(3-Cl-pyridinyl)	161–163
417	*i*-Pr	H	2-Me	Me	2-(3-Cl-pyridinyl)	193–195
418	Me	H	2-Me	Me	2-(3-Cl-pyridinyl)	194–196
419	*i*-Pr	H	2-Me-4-Cl	CN	2-(3-Cl-pyridinyl)	188–190
420	*t*-Bu	H	2-Me-4-Cl	CN	2-(3-Cl-pyridinyl)	148–151
421	Me	H	2-Me-4-Cl	CN	2-(3-Cl-pyridinyl)	182–184
422	Me	H	2-Me	Br	2-(3-Cl-pyridinyl)	210–212
423	H	H	2-Cl	CF_3	2-Cl-Ph	203–205
424	H	H	2-Me-4-Br	CF_3	2-(3-Cl-pyridinyl)	243–245
425	*t*-Bu	H	2-Me	CF_3	5-(1,3-di-Me-4-Cl-pyrazolyl)	220-221
426	*i*-Pr	H	2-Cl	CF_3	5-(1,3-di-Me-4-Cl-pyrazolyl)	264-266

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
427	*t*-Bu	H	2-Cl	CF_3	5-(1,3-di-Me-4-Cl-pyrazolyl)	231-232
428	CH_2CN	H	2-Br-4-Me	CF_3	2-(3-Cl-pyridinyl)	149–150
429	*i*-Pr	H	2-Me-4-Cl	Cl	2-Cl-Ph	180–181
430	*i*-Pr	H	2-Me-4-Br	Br	2,6-di-Cl-Ph	238–239
431	*i*-Pr	H	2-Cl-4-Me	CF_3	2-(3-Cl-pyridinyl)	170–171
432	*t*-Bu	H	2-Cl-4-Me	CF_3	2-(3-Cl-pyridinyl)	167–169
433	Me	H	2-Cl-4-Me	CF_3	2-(3-Cl-pyridinyl)	162–164
434	H	H	2-Me-4-Br	Br	2-(3-Cl-pyridinyl)	235–237
435	Me	H	5-Cl	CF_3	2-(3-Cl-pyridinyl)	207–208
436	CH_2CN	H	5-Cl	CF_3	2-(3-Cl-pyridinyl)	178–179
437	Me	H	5-Me	CF_3	2-(3-Cl-pyridinyl)	166–167
438	CH_2CN	H	5-Me	CF_3	2-(3-Cl-pyridinyl)	191–192
439	H	H	2-Me-4-Br	CF_3	2-(3-Cl-pyridinyl)	243–244
440	*i*-Pr	H	2-Me	CF_3	4-pyrimidinyl	
441	*i*-Pr	H	2-Cl	CF_3	4-pyrimidinyl	
442	*t*-Bu	H	2-Me	CF_3	4-pyrimidinyl	
443	*t*-Bu	H	2-Cl	CF_3	4-pyrimidinyl	
444	*i*-Pr	H	2,3-di-Me	CF_3	2-(3-Cl-pyridinyl)	173–175
445	*t*-Bu	H	2,3-di-Me	CF_3	2-(3-Cl-pyridinyl)	149–150
446	Me	H	2,3-di-Me	CF_3	2-(3-Cl-pyridinyl)	164–166
447	H	H	2,3-di-Me	CF_3	2-(3-Cl-pyridinyl)	201–203
448	H	H	2-Cl-4-Br	CF_3	2-(3-Cl-pyridinyl)	240–242
449	H	H	2-Cl-4-Me	CF_3	2-(3-Cl-pyridinyl)	223–225
450	*i*-Pr	H	2-Me	CF_3	4-(5-Cl-pyrimidinyl)	
451	*t*-Bu	H	2-Me	CF_3	4-(5-Cl-pyrimidinyl)	
452	*t*-Bu	H	2-Cl	CF_3	4-(5-Cl-pyrimidinyl)	
453	*c*-Pr	H	2-Cl	CF_3	2-(3-Cl-pyridinyl)	224–228
454	CH_2CN	H	2-Me-4-Br	Br	2-(3-Cl-pyridinyl)	232–234
455	CH_2CN	H	2-Me-4-I	CF_3	2-(3-Cl-pyridinyl)	221–222
456	Me	H	2,4-di-Cl	CF_3	2-Cl-Ph	232–233
457	Et	H	2,4-di-Cl	CF_3	2-Cl-Ph	247–248
458	*t*-Bu	H	2,4-di-Cl	CF_3	2-Cl-Ph	223–224
459	CH_2CN	H	2,4-di-Cl	CF_3	2-Cl-Ph	229–231
460	*i*-Pr	H	2-Me	CF_3	5-(1-Me-pyrazolyl)	240-241
461	*t*-Bu	H	2-Me	CF_3	5-(1-Me-pyrazolyl)	233-234
462	*i*-Pr	H	2-Cl	CF_3	5-(1-Me-pyrazolyl)	247-248

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
463	*t*-Bu	H	2-Cl	CF_3	5-(1-Me-pyrazolyl)	262-263
464	*i*-Pr	H	2-Me	CF_3	4-(2,6-di-Me-5-Cl-pyrimidinyl)	
465	*i*-Pr	H	2-Cl	CF_3	4-(2,6-di-Me-5-Cl-pyrimidinyl)	
466	*t*-Bu	H	2-Me	CF_3	4-(2,6-di-Me-5-Cl-pyrimidinyl)	
467	*t*-Bu	H	2-Cl	CF_3	4-(2,6-di-Me-5-Cl-pyrimidinyl)	
468	Et	H	2-Me	Cl	2-(3-Cl-pyridinyl)	220-221
469	Me	H	2-Me	Cl	2-(3-Cl-pyridinyl)	217–218
470	$CH_2C≡CH$	H	2,4-di-Br	Cl	2-(3-Cl-pyridinyl)	199–201
471	$CH_2C≡CH$	H	2-Me-4-Cl	Cl	2-(3-Cl-pyridinyl)	219–221
472	H	H	2-Me-4-Cl	Cl	2-(3-Cl-pyridinyl)	231–233
473	H	H	2,4-di-Cl	Cl	2-(3-Cl-pyridinyl)	245–247
474	$CH_2C≡CH$	H	2,4-di-Cl	Cl	2-(3-Cl-pyridinyl)	166–168
475	H	H	2-Me	Cl	2-(3-Cl-pyridinyl)	243–244
476	H	H	2-Me-4-I	CF_3	2-(3-Cl-pyridinyl)	241–242
477	CH_2CN	H	2-Me-4-Cl	Br	2-(3-Cl-pyridinyl)	225–226
478	$CH_2C≡CH$	H	2-Me-4-Br	Cl	2-(3-Cl-pyridinyl)	218–220
479	H	H	2-Me-4-Br	Cl	2-(3-Cl-pyridinyl)	224–225
480	H	H	2,4-di-Br	Cl	2-(3-Cl-pyridinyl)	250–252
481	*i*-Pr	H	2-Me-4-Cl	CF_3	2-(3-Me-pyridinyl)	228–229
482	Me	H	2-Me-4-Cl	CF_3	2-(3-Me-pyridinyl)	226–227
483	*t*-Bu	H	2-Me	CF_3	5-(1-Me-4-Cl-pyrazolyl)	216-217
484	*i*-Pr	H	2-Me	CF_3	5-(1-Me-4-Cl-pyrazolyl)	220-221
485	*i*-Pr	H	2-Me-4-($HOCH_2$)	CF_3	2-(3-Cl-pyridinyl)	199–201
486	$CH_2C≡CH$	H	2-Me-4-Cl	CF_3	2-(3-Cl-pyridinyl)	200–202
487	*i*-Pr, B is S	H	2-Me-4-Br	CF_3	2-(3-Cl-pyridinyl)	214–217
488	*i*-Pr	H	2-Me-4-CO_2Me	CF_3	2-(3-Cl-pyridinyl)	204-206
489	*i*-Pr	H	2-Me-4-CONHMe	CF_3	2-(3-Cl-pyridinyl)	168-170
490	$CH(CH_3)Ph$	H	H	CF_3	Me	212-214
491	$CH(CH_3)Ph$	H	H	CF_3	Et	202-203
492	CH_2CH_2N(*i*-Pr)	H	2-Me	CF_3	2-Cl-Ph	188-190

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
494	*i*-Pr	H	2-Me-4-Br	CF_3	2-(3-Cl-pyridinyl)	197-198
495	*i*-Pr	H	2-Me	CF_3	2-CH_2NHC(=O)CF_3-Ph	*
496	*i*-Pr	H	2-Me	CF_3	2-CH_2NH_2-Ph HCl	*
497 (Ex. 6)	*i*-Pr	H	2-Me-4-Cl	CF_3	2-(3-Cl-pyridinyl)	196-197
498	*i*-Pr	H	2-Me	CF_3	2,4-di-Cl-5-OCH_2C≡CH-Ph	246-249
499	*t*-Bu	H	2-Me-4-Cl	CF_3	2-(3-Cl-pyridinyl)	223-225
500 (Ex. 7)	Me	H	2-Me-4-Cl	CF_3	2-(3-Cl-pyridinyl)	148-150
501	*i*-Pr	H	2,4-di-Br	CF_3	2-(3-Cl-pyridinyl)	192-193
502	*t*-Bu	H	2,4-di-Br	CF_3	2-(3-Cl-pyridinyl)	246-247
505	$CH_2CH_2OCH_2CH_2OH$	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	132-135
506	Me	H	2,4-di-Br	CF_3	2-(3-Cl-pyridinyl)	162-163
507	$OCH(CH_3)_2$	H	2-Cl	CF_3	2-Cl-Ph	218-219
508	$OCH(CH_3)_2$	H	2-Cl	CF_3	2-(3-Cl-pyridinyl)	205-206
509	$OCH(CH_3)_2$	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	210-211
510	$OCH(CH_3)_2$	H	2-Me	CF_3	2-Cl-Ph	196-198
511	*i*-Pr	H	2-Me	CF_3	2-CONHMe-Ph	*
512	Et	H	2,4-di-Br	CF_3	2-(3-Cl-pyridinyl)	188-189
513	*i*-Pr	H	2,4-di-Cl	CF_3	2-(3-Cl-pyridinyl)	200-201
514	*t*-Bu	H	2,4-di-Cl	CF_3	2-(3-Cl-pyridinyl)	170-172
515	Me	H	2,4-di-Cl	CF_3	2-(3-Cl-pyridinyl)	155-157
516	Et	H	2,4-di-Cl	CF_3	2-(3-Cl-pyridinyl)	201-202
517	*t*-Bu	H	2-Me-4-Br	CF_3	2-(3-Cl-pyridinyl)	247-248
518	Et	H	2-Me-4-Br	CF_3	2-(3-Cl-pyridinyl)	192-193
519	*i*-Pr	H	2-Me-4-F	CF_3	2-(3-Cl-pyridinyl)	179-180
520	*i*-Pr	H	2-Me-4-Br	Br	2-(3-Cl-pyridinyl)	185-187
521	*i*-Pr	H	2-Me-4-CF_3	CF_3	2-(3-Cl-pyridinyl)	235-236
522	Et	H	2-Me-4-CF_3	CF_3	2-(3-Cl-pyridinyl)	216-217
523	*i*-Pr	H	2-Me-4-I	CF_3	2-(3-Cl-pyridinyl)	188-189
524	*t*-Bu	H	2-Me-4-CF_3	CF_3	2-(3-Cl-pyridinyl)	148-149
525	Me	H	2-Me-4-Br	CF_3	2-(3-Cl-pyridinyl)	208-210
526	*i*-Pr	H	2-Br-4-Me	CF_3	2-(3-Cl-pyridinyl)	127-128
527	*t*-Bu	H	2-Br-4-Me	CF_3	2-(3-Cl-pyridinyl)	159-160
528	Et	H	2-Br-4-Me	CF_3	2-(3-Cl-pyridinyl)	224-225
529	Me	H	2-Br-4-Me	CF_3	2-(3-Cl-pyridinyl)	208-209
530 (Ex. 10)	*i*-Pr	H	2-Me-4-Cl	Br	2-(3-Cl-pyridinyl)	159-161

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
531 (Ex. 11)	Me	H	2-Me-4-Cl	Br	2-(3-Cl-pyridinyl)	162-164
532	*t*-Bu	H	2-Me-4-Cl	Br	2-(3-Cl-pyridinyl)	159-161
533	*i*-Pr	H	2,4-di-Br	Br	2-(3-Cl-pyridinyl)	162-163
534	Me	H	2,4-di-Br	Br	2-(3-Cl-pyridinyl)	166-168
535	*t*-Bu	H	2,4-di-Br	Br	2-(3-Cl-pyridinyl)	210-212
536	*i*-Pr	H	2,4-di-Cl	Br	2-(3-Cl-pyridinyl)	188-190
537	Me	H	2,4-di-Cl	Br	2-(3-Cl-pyridinyl)	179-180
538	Me	H	2-Me-4-Br	Br	2-(3-Cl-pyridinyl)	147-149
539	*i*-Pr	H	2-Cl-4-Br	CF_3	2-(3-Cl-pyridinyl)	200-202
540	*t*-Bu	H	2-Cl-4-Br	CF_3	2-(3-Cl-pyridinyl)	143-145
541	Me	H	2-Cl-4-Br	CF_3	2-(3-Cl-pyridinyl)	171-173
542	Me	H	2-Me-4-Br	CF_3	2-(3-Cl-pyridinyl)	222-223
543 (Ex. 8)	*i*-Pr	H	2-Me-4-Cl	Cl	2-(3-Cl-pyridinyl)	142-144
544 (Ex. 9)	Me	H	2-Me-4-Cl	Cl	2-(3-Cl-pyridinyl)	175-177
545	*t*-Bu	H	2-Me-4-Cl	Cl	2-(3-Cl-pyridinyl)	163-165
546	*i*-Pr	H	2-Me-4-Br	Cl	2-(3-Cl-pyridinyl)	152-153
547	Me	H	2-Me-4-Br	Cl	2-(3-Cl-pyridinyl)	140-141
548	*t*-Bu	H	2-Me-4-Br	Br	2-(3-Cl-pyridinyl)	215-221
549	Me	H	2-Me-4-I	CF_3	2-(3-Cl-pyridinyl)	199-200
550	*i*-Pr	H	2,4-di-Br	Cl	2-(3-Cl-pyridinyl)	197-199
551	Me	H	2,4-di-Br	Cl	2-(3-Cl-pyridinyl)	188-190
552	*t*-Bu	H	2,4-di-Br	Cl	2-(3-Cl-pyridinyl)	194-196
553	Et	H	2,4-di-Br	Cl	2-(3-Cl-pyridinyl)	192-194
554	*i*-Pr	H	2,4-di-Cl	Cl	2-(3-Cl-pyridinyl)	197-199
555	Me	H	2,4-di-Cl	Cl	2-(3-Cl-pyridinyl)	205-206
556	*t*-Bu	H	2,4-di-Cl	Cl	2-(3-Cl-pyridinyl)	172-173
557	Et	H	2,4-di-Cl	Cl	2-(3-Cl-pyridinyl)	206-208
558	Et	H	2-Me-4-Cl	Cl	2-(3-Cl-pyridinyl)	199-200
559	Et	H	2-Me-4-Cl	CF_3	2-(3-Cl-pyridinyl)	163-164
560	Et	H	2-Me-4-I	CF_3	2-(3-Cl-pyridinyl)	199-200
561	*t*-Bu	H	2-Me-4-I	CF_3	2-(3-Cl-pyridinyl)	242-243
562	Et	H	2-Me-4-Cl	Br	2-(3-Cl-pyridinyl)	194-195
563	Me	H	2-Me-4-F	CF_3	2-(3-Cl-pyridinyl)	213-214
564	Et	H	2-Me-4-F	CF_3	2-(3-Cl-pyridinyl)	212-213
565	*t*-Bu	H	2-Me-4-F	CF_3	2-(3-Cl-pyridinyl)	142-143
566	Me	H	2-Me-4-F	Br	2-(3-Cl-pyridinyl)	214-215
567	Et	H	2-Me-4-F	Br	2-(3-Cl-pyridinyl)	204-205

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
568	*i*-Pr	H	2-Me-4-F	Br	2-(3-Cl-pyridinyl)	206-208
569	Et	H	2-Me-4-Br	Cl	2-(3-Cl-pyridinyl)	192-194
570	*i*-Pr	H	2-Me-4-F	Cl	2-(3-Cl-pyridinyl)	184-186
571	Me	H	2-Me-4-F	Cl	2-(3-Cl-pyridinyl)	180-182
572	Et	H	2-Me-4-F	Cl	2-(3-Cl-pyridinyl)	163-165
573	*t*-Bu	H	2-Me-4-Br	Cl	2-(3-Cl-pyridinyl)	224-225
574	*t*-Bu	H	2-Me-4-F	Br	2-(3-Cl-pyridinyl)	124-125
575	Et	H	2,4-di-Br	Br	2-(3-Cl-pyridinyl)	196-197
576	Me	H	2,4-di-Cl	Br	2-(3-Cl-pyridinyl)	245-246
577	Et	H	2,4-di-Cl	Br	2-(3-Cl-pyridinyl)	214-215
578	Et	H	2-Me-4-Br	Br	2-(3-Cl-pyridinyl)	194-196
579	Me	H	2-Me-4-I	Br	2-(3-Cl-pyridinyl)	229-230
580	*i*-Pr	H	2-Me-4-I	Br	2-(3-Cl-pyridinyl)	191-192
581	Me	H	2-Me-4-CF_3	CF_3	2-(3-Cl-pyridinyl)	249-250
582	Me	H	2-Me-4-I	Cl	2-(3-Cl-pyridinyl)	233-235
583	Et	H	2-Me-4-I	Cl	2-(3-Cl-pyridinyl)	196-197
584	*i*-Pr	H	2-Me-4-I	Cl	2-(3-Cl-pyridinyl)	189-190
585	*t*-Bu	H	2-Me-4-I	Cl	2-(3-Cl-pyridinyl)	228-229
586	Me	H	2-Me-4-Cl	I	2-(3-Cl-pyridinyl)	208-209
587	*i*-Pr	H	2-Me-4-Cl	I	2-(3-Cl-pyridinyl)	183-184
588	H	H	2-Me-4-Cl	I	2-(3-Cl-pyridinyl)	228-230
589	Me	H	2-Me-4-Cl	Br	2-Cl-4-F-Ph	250-251
590	H	H	2-Me-4-Cl	Br	2-Cl-4-F-Ph	229-229
591	*i*-Pr	H	2-Me-4-Cl	Br	2-Cl-4-F-Ph	189-190
592	*t*-Bu	H	2-Me-4-Cl	Br	2-Cl-4-F-Ph	247-249
593	*i*-Pr	H	2-Me-4-NO_2	CF_3	2-Cl-Ph	*
594	Ph	H	2-Me-4-Cl	CF_3	2-(3-Cl-pyridinyl)	243-244
595	2-Me-Ph	H	2-Me-4-Cl	CF_3	2-(3-Cl-pyridinyl)	249-251
596	*i*-Pr	H	2-Me-4-NO_2	CF_3	2-(3-Cl-pyridinyl)	170-172
597	*i*-Pr	H	2-Me-4-NO_2	CF_3	2-(3-Cl-pyridinyl)	*
598	Me, B is S	H	2-Me	CF_3	2-Cl-Ph	164-167
599	*i*-Pr	H	2-NO_2	CF_3	2-Cl-Ph	*
600	*i*-Pr	H	2-Me-4-Cl	$OCHF_2$	2-Cl-Ph	177-179
601	Me	Me	2,4-di-Br	Cl	2-(3-Cl-pyridinyl)	151-152
602	$CH(CH_3)CH_2OCH_3$	H	2,4-di-Br	Cl	2-(3-Cl-pyridinyl)	162-163
603	$CH(CH_3)CH_2SCH3$	H	2,4-di-Br	Cl	2-(3-Cl-pyridinyl)	174-175
604	$CH(CH_3)CH_2OH$	H	2,4-di-Br	Cl	2-(3-Cl-pyridinyl)	148-149

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
605	*i*-Pr, R1 is Me	H	2-Me	Br	2-(3-Cl-pyridinyl)	223-225
606	*i*-Pr, R1 is Me	H	2-Me	Cl	2-(3-Cl-pyridinyl)	223-225
607	*i*-Pr, R1 is Me	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	218-219
608	*i*-Pr, B is S	H	2-Me-4-Cl	Br	2-(3-Cl-pyridinyl)	231-235
609	$N(CH_3)_2$	H	2,4-di-Br	Cl	2-(3-Cl-pyridinyl)	149-151
611	$N(Me)_2$	H	2-Me-4-Cl	Br	2-(3-Cl-pyridinyl)	185-188
612	*i*-Pr	H	2-Cl	CF_3	5-(1-Me-4-Cl-pyrazolyl)	221-222
613	*t*-Bu	H	2-Cl	CF_3	5-(1-Me-4-Cl-pyrazolyl)	217-218
614	$CH(CH_3)CH_2CO_2Et$	H	2,4-di-Br	Cl	2-(3-Cl-pyridinyl)	113-115
615	2-pyridinyl	H	2-Me-4-Br	CF_3	2-(3-Cl-pyridinyl)	244-245
616	2-(3-Me-pyridinyl)	H	2-Me-4-Br	CF_3	2-(3-Me-pyridinyl)	182-183
619	Me, B is S	H	2-Me-4-Cl	Br	2-(3-Cl-pyridinyl)	110-113
620	Me	Me	2-Me-4-Br	CF_3	2-(3-Cl-pyridinyl)	207-208
621	Et	Et	2-Me-4-Br	CF_3	2-(3-Cl-pyridinyl)	189-190
622	2-pyridinyl	H	2-Me-4-Cl	CF_3	2-(3-Cl-pyridinyl)	233-234
623	2-(3-Me-pyridinyl)	H	2-Me-4-Cl	CF_3	2-(3-Cl-pyridinyl)	202-203
624	Et	Et	2,4-di-Cl	Cl	2-(3-Cl-pyridinyl)	197-198
625	Me	Me	2,4-di-Cl	Cl	2-(3-Cl-pyridinyl)	142-143
626	$CH(CH_3)CH_2SCH_3$	H	2,4-di-Cl	Cl	2-(3-Cl-pyridinyl)	185-186
627	Et	Et	2,4-di-Br	Cl	2-(3-Cl-pyridinyl)	209-210
628	*i*-Pr	Me	2-Me-4-Br	CF_3	2-(3-Cl-pyridinyl)	133-135
629	Me	Me	2,4-di-Br	Br	2-(3-Cl-pyridinyl)	185-187
630	Et	Et	2,4-di-Br	Br	2-(3-Cl-pyridinyl)	204-205
631	$CH(CH_3)CH_2SCH_3$	H	2,4-di-Br	Br	2-(3-Cl-pyridinyl)	178-179
632	Et	H	2-Me-4-Cl	$OCHF_2$	2-(3-Cl-pyridinyl)	209-211
633	*i*-Pr	H	2-Me-4-Cl	$OCHF_2$	2-(3-Cl-pyridinyl)	179-181
634	Me	H	2-Me-4-Br	$OCHF_2$	2-(3-Cl-pyridinyl)	190-192
635	Et	H	2-Me-4-Cl	OEt	2-Cl-Ph	163-165
636	*i*-Pr	H	2-Me-4-Cl	OEt	2-Cl-Ph	173-175
637	Me	H	2-Me-4-Br	OEt	2-Cl-Ph	155-158
638	Et	Me	2,4-di-Br	Br	2-(3-Cl-pyridinyl)	181-183
639	Et	Me	2,4-di-Cl	Cl	2-(3-Cl-pyridinyl)	162-163
640	Et	Me	2-Me-4-Br	CF_3	2-(3-Cl-pyridinyl)	174-175
641	Me	Me	2,4-di-Cl	Br	2-(3-Cl-pyridinyl)	216-218
642	Et	Et	2,4-di-Cl	Br	2-(3-Cl-pyridinyl)	190-191
643	$CH(CH_3)CH_2SCH_3$	H	2,4-di-Cl	Br	2-(3-Cl-pyridinyl)	182-183
644	Et	Me	2,4-di-Cl	Br	2-(3-Cl-pyridinyl)	165-167

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
645	Et	H	2-Me-4-NO_2	CF_3	2-(3-Cl-pyridinyl)	*
646	Me	Me	2-Me-4-NO_2	CF_3	2-(3-Cl-pyridinyl)	*
647	$CH_2CH{=}CH_2$	H	2-Me-4-NO_2	CF_3	2-(3-Cl-pyridinyl)	*
648	*n*-Pr	H	2-Me-4-NO_2	CF_3	2-(3-Cl-pyridinyl)	*
649	$CH(CH_3)CH_2SCH_3$	H	2-Me-4-NO_2	CF_3	2-(3-Cl-pyridinyl)	*
650	Me	H	2-Me-4-NO_2	CF_3	2-(3-Cl-pyridinyl)	*
651	*t*-Bu	H	2-Me-4-NO_2	CF_3	2-(3-Cl-pyridinyl)	*
652	$CH_2CH_2N(Me)_2$	H	2-Me-4-NO_2	CF_3	2-(3-Cl-pyridinyl)	193-195
653	$CH_2CH_2N(Me)_3^+ I^-$	H	2-Me-4-NO2	CF_3	2-(3-Cl-pyridinyl)	>250
655	$N(CH_3)_2$	H	2,4-di-Cl	Cl	2-(3-Cl-pyridinyl)	146-148
656	$N(CH_3)_2$	H	2,4-di-Br	Br	2-(3-Cl-pyridinyl)	162-164
657	$N(CH_3)_2$	H	2,4-di-Cl	Br	2-(3-Cl-pyridinyl)	208-209
658	Et	H	2-Me-4-Cl	OCH_2CF_3	2-Cl-Ph	184-186
659	*i*-Pr	H	2-Me-4-Cl	OCH_2CF_3	2-Cl-Ph	196-198
660	Me	H	2-Me-4-Br	OCH_2CF_3	2-Cl-Ph	220-223
661	$N(CH_3)_2$	H	2-Me-4-NO2	CF_3	2-(3-Cl-pyridinyl)	*
662	H	H	2-Me-4-Cl	Br	2-(3-Cl-pyridinyl)	240-242
663	*n*-Pr	*n*-Pr	2-Me-4-Br	CF_3	2-(3-Cl-pyridinyl)	201-202
664	*n*-Pr	H	2-Me-4-Br	CF_3	2-(3-Cl-pyridinyl)	188-190
665	Et	Et	2-Cl	CF_3	2-(3-Cl-pyridinyl)	242-243
666	*n*-Pr	*n*-Pr	2,4-di-Cl	Cl	2-(3-Cl-pyridinyl)	242-243
667	*n*-Pr	H	2,4-di-Cl	Cl	2-(3-Cl-pyridinyl)	218-219
668	$CH_2CO_2CH_2CH_3$	Me	2-Me-4-Br	CF_3	2-(3-Cl-pyridinyl)	227-228
669	$CH_2CO_2CH_2CH_3$	Me	2,4-di-Cl	Br	2-(3-Cl-pyridinyl)	176-177
670	$CH_2CO_2CH_2CH_3$	Me	2,4-di-Br	Cl	2-(3-Cl-pyridinyl)	198-199
671	$CH_2CO_2CH_3$	H	2-Me-4-Br	CF_3	2-(3-Cl-pyridinyl)	141-142
672	$N(CH_3)_2$	H	2,4-di-Cl	CF_3	2-(3-Cl-pyridinyl)	136-137
673	Me	Me	2,4-di-Cl	CF_3	2-(3-Cl-pyridinyl)	225-227
674	Et	Et	2,4-di-Cl	CF_3	2-(3-Cl-pyridinyl)	228-229
675	$CH_2CO_2CH_2CH_3$	Me	2,4-di-Cl	CF_3	2-(3-Cl-pyridinyl)	219-220
676	Me	H	2-Me-4-Cl	CF_3	5-(1-Me-4-Cl-pyrazolyl)	239-241
677	*i*-Pr	H	2-Me-4-Cl	CF_3	5-(1-Me-4-Cl-pyrazolyl)	252-254
678	*i*-Pr	H	2-Me-4-Br	OEt	2-(3-Cl-pyridinyl)	208-211
679	Me	H	2-Me-4-Br	OEt	2-(3-Cl-pyridinyl)	212-215
680	*i*-Pr	H	2-Me-4-Cl	OEt	2-(3-Cl-pyridinyl)	191-193
681	Et	H	2-Me-4-Cl	OEt	2-(3-Cl-pyridinyl)	207-209
682	*i*-Pr	H	2-Me-4-Br	OCH_2CF_3	2-(3-Cl-pyridinyl)	213-215

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
683	Me	H	2-Me-4-Br	OCH_2CF_3	2-(3-Cl-pyridinyl)	206-208
684	*i*-Pr	H	2-Me-4-Cl	OCH_2CF_3	2-(3-Cl-pyridinyl)	211-213
685	Et	H	2-Me-4-Cl	OCH_2CF_3	2-(3-Cl-pyridinyl)	205-207
686 (Ex. 12)	Me	H	2-Me-4-Cl	OCH_2CF_3	2-(3-Cl-pyridinyl)	195-197
687	Et	H	2-Me-4-Br	OCH_2CF_3	2-(3-Cl-pyridinyl)	208-211
688	*t*-Bu	H	2-Me-4-Br	OCH_2CF_3	2-(3-Cl-pyridinyl)	213-216
689	*i*-Pr	H	2-Me-4-Br	CF_3	5-(1-Me-4-Cl-pyrazolyl)	256-258
690	*t*-Bu	H	2-Me-4-Br	CF_3	5-(1-Me-4-Cl-pyrazolyl)	254-256
691	Me	Me	2,4-di-Br	CF_3	2-(3-Cl-pyridinyl)	228-229
692	*i*-Pr	H	2-Me-4-Cl	OCF_2CHF_2	2-(3-Cl-pyridinyl)	189-192
693	Et	H	2-Me-4-Cl	OCF_2CHF_2	2-(3-Cl-pyridinyl)	189-192
694	Me	H	2-Me-4-Cl	OCF_2CHF_2	2-(3-Cl-pyridinyl)	162-165
695	*i*-Pr	H	2-Me-4-Br	OCF_2CHF_2	2-(3-Cl-pyridinyl)	185-188
696	Et	H	2-Me-4-Br	OCF_2CHF_2	2-(3-Cl-pyridinyl)	195-198
697	Me	H	2-Me-4-Br	OCF_2CHF_2	2-(3-Cl-pyridinyl)	164-167
698	Me	Me	2-Cl-4-Br	CF_3	2-(3-Cl-pyridinyl)	238-239
699	Et	Me	2-Cl-4-Br	CF_3	2-(3-Cl-pyridinyl)	216-217
700	H	H	H	CF_3	2-(3-Cl-pyridinyl)	
701	Et	H	2-Me-4-Br	CF_3	5-(1-Me-4-Cl-pyrazolyl)	249-251
702	*i*-Pr	H	2,4-di-Cl	OCH_2CF3	2-(3-Cl-pyridinyl)	232-235
703	Me	H	2,4-di-Cl	OCH_2CF_3	2-(3-Cl-pyridinyl)	192-195
704	Me	Me	2,4-di-Cl	OCH_2CF_3	2-(3-Cl-pyridinyl)	132-135
705	*i*-Pr	H	2,4-di-Br	OCH_2CF_3	2-(3-Cl-pyridinyl)	225-227
706	Me	H	2,4-di-Br	OCH_2CF_3	2-(3-Cl-pyridinyl)	206-208
707	Me	Me	2,4-di-Br	OCH_2CF_3	2-(3-Cl-pyridinyl)	175-177
708	Me	H	2-Cl-4-Br	Br	2-(3-Cl-pyridinyl)	226-227
709	Me	Me	2-Cl-4-Br	Br	2-(3-Cl-pyridinyl)	237-238
710	Me	H	2-Cl-4-Br	Cl	2-(3-Cl-pyridinyl)	228-229
711	Me	Me	2-Cl-4-Br	Cl	2-(3-Cl-pyridinyl)	236-237
712	$CH_2C(Me)_2CH_2N$-$(Me)_2$	H	2-Me	CF_3	2-(3-Cl-pyridinyl)	197-200
713	Me	H	2-Me-4-Br	CF_3	5-(1-Me-4-Cl-pyrazolyl)	242-244
714	Et	H	2-Me-4-Cl	CF_3	5-(1-Me-4-Cl-pyrazolyl)	252-254
715	*t*-Bu	H	2-Me-4-Cl	CF_3	5-(1-Me-4-Cl-pyrazolyl)	259-260
716	*i*-Pr	H	2,4-di-Cl	$OCBrF_2$	2-(3-Cl-pyridinyl)	220-222
717	Me	H	2,4-di-Cl	$OCBrF_2$	2-(3-Cl-pyridinyl)	188-191
718	Me	Me	2,4-di-Cl	$OCBrF_2$	2-(3-Cl-pyridinyl)	203-205

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
719	Me	H	2-Me-4-Cl	$OCHF_2$	2-(3-Cl-pyridinyl)	210-212
720	*i*-Pr	H	2-Me-4-Cl	$OCBrF_2$	2-(3-Cl-pyridinyl)	194-196
721	Me	H	2-Me-4-Cl	$OCBrF_2$	2-(3-Cl-pyridinyl)	181-183
722	Me	H	3,4-di-F	Cl	2-(3-Cl-pyridinyl)	202-203
723	Me	Me	3,4-di-F	Cl	2-(3-Cl-pyridinyl)	251-252
724	Me	Me	2-Me-4-F	Cl	2-(3-Cl-pyridinyl)	242-243
725	Me	Me	2-Cl-4-F	Br	2-(3-Cl-pyridinyl)	245-246
726	Me	H	2-Cl-4-F	Br	2-(3-Cl-pyridinyl)	217-218
727	*i*-Pr	H	2-Cl-4-F	Br	2-(3-Cl-pyridinyl)	168-169
728	Me	Me	2-Cl-4-F	Cl	2-(3-Cl-pyridinyl)	239-240
729	Me	H	2-Cl-4-F	Cl	2-(3-Cl-pyridinyl)	248-249
730	*i*-Pr	H	2-Cl-4-F	Cl	2-(3-Cl-pyridinyl)	169-170
731	Me	Me	2-Cl-4-F	CF_3	2-(3-Cl-pyridinyl)	215-216
732	Me	H	2-Cl-4-F	CF_3	2-(3-Cl-pyridinyl)	219-220
733	Me	Me	2-Br-4-F	Br	2-(3-Cl-pyridinyl)	235-236
734	Me	H	2-Br-4-F	Br	2-(3-Cl-pyridinyl)	238-239
735	*i*-Pr	H	2-Br-4-F	Br	2-(3-Cl-pyridinyl)	236-237
736	Me	Me	2-Br-4-F	Cl	2-(3-Cl-pyridinyl)	246-247
737	Me	H	2-Br-4-F	Cl	2-(3-Cl-pyridinyl)	233-234
738	*i*-Pr	H	2-Br-4-F	Cl	2-(3-Cl-pyridinyl)	153-154
739	*i*-Pr	H	2-Me-4-Cl	$OCHMe_2$	2-(3-Cl-pyridinyl)	208-210
740	Me	H	2-Me-4-Cl	$OCHMe_2$	2-(3-Cl-pyridinyl)	207-210
741	*i*-Pr	H	2,4-di-Cl	$OCHMe_2$	2-(3-Cl-pyridinyl)	187-191
742	Me	H	2,4-di-Cl	$OCHMe_2$	2-(3-Cl-pyridinyl)	*
743	Me	Me	2-Br-4-F	CF_3	2-(3-Cl-pyridinyl)	191-192
744	Me	H	2-Br-4-F	CF_3	2-(3-Cl-pyridinyl)	228-229
745	*i*-Pr	H	2-Br-4-F	CF_3	2-(3-Cl-pyridinyl)	224-226
746	Me	Me	2-Br-4-Cl	Br	2-(3-Cl-pyridinyl)	188-189
747	Me	H	2-Br-4-Cl	Br	2-(3-Cl-pyridinyl)	248-249
748	*i*-Pr	H	2-Br-4-Cl	Br	2-(3-Cl-pyridinyl)	252-253
749	Me	Me	2-Br-4-Cl	Cl	2-(3-Cl-pyridinyl)	147-148
750	Me	H	2-Br-4-Cl	Cl	2-(3-Cl-pyridinyl)	249-250
751	*i*-Pr	H	2-Br-4-Cl	Cl	2-(3-Cl-pyridinyl)	239-240
752	Me	Me	2-Br-4-Cl	CF_3	2-(3-Cl-pyridinyl)	200-201
753	Me	H	2-Br-4-Cl	CF_3	2-(3-Cl-pyridinyl)	158-159
754	*i*-Pr	H	2-Br-4-Cl	CF_3	2-(3-Cl-pyridinyl)	250-250
755	Me	Me	2-Me-4-Cl	Cl	2-(3-Cl-pyridinyl)	232-233

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
756	Me	H	2-CF_3	CF_3	2-(3-Cl-pyridinyl)	218-220
757	*i*-Pr	H	2-CF_3	CF_3	2-(3-Cl-pyridinyl)	242-246
758	Me	Me	2-CF_3	CF_3	2-(3-Cl-pyridinyl)	239-244
759	Me	Me	2-Me-4-Cl	Br	2-(3-Cl-pyridinyl)	210-211
760	Me	Me	2,4-di-Me	Cl	2-(3-Cl-pyridinyl)	223-224
761	Me	Me	2,4-di-Me	Br	2-(3-Cl-pyridinyl)	240-241
762	Me	H	2-F	Br	2-(3-Cl-pyridinyl)	215-216
763	*i*-Pr	H	2-F	Br	2-(3-Cl-pyridinyl)	213-215
764	*i*-Pr	H	2-CF_3-4-Cl	CF_3	2-(3-Cl-pyridinyl)	254-256
765	Me	Me	2-CF_3-4-Cl	CF_3	2-(3-Cl-pyridinyl)	229-231
766	Me	H	2-CF_3-4-Cl	CF_3	2-(3-Cl-pyridinyl)	235-237
767	Me	H	2,4-di-Cl	CF_3	2-(3-Cl-pyridinyl), R^8 is Cl	225-226
768	*i*-Pr	H	2,4-di-Cl	CF_3	2-(3-Cl-pyridinyl), R^8 is Cl	230-232
769	Me	Me	2,4-di-Cl	CF_3	2-(3-Cl-pyridinyl), R^8 is Cl	194-196
770	*i*-Pr	H	2-Me-4-Cl	CF_3	3-isoxazolyl	255-257
771	Me	H	2,4-di-F	Br	2-(3-Cl-pyridinyl)	197-198
772	Me	Me	2,4-di-F	Br	2-(3-Cl-pyridinyl)	218-222
773	Me	H	2-F	Cl	2-(3-Cl-pyridinyl)	185-187
774	Me	H	2-F-4-Cl	Br	2-(3-Cl-pyridinyl)	203-204
775	Me	Me	2-F-4-Cl	Br	2-(3-Cl-pyridinyl)	226-227
776	*i*-Pr	H	2-F-4-Cl	Br	2-(3-Cl-pyridinyl)	207-208
777	Me	H	2-F-4-Cl	Cl	2-(3-Cl-pyridinyl)	211-212
778	Me	Me	2-F, 4-Cl	Cl	2-(3-Cl-pyridinyl)	237-238
779	*i*-Pr	H	2-Me-4-CN	CF_3	2-(3-Cl-pyridinyl)	*
780	H	H	2-F-4-Cl	Cl	2-(3-Cl-pyridinyl)	116-117
781	Me	H	2,4-di-F	Cl	2-(3-Cl-pyridinyl)	159-160
782	Me	Me	2,4-di-F	Cl	2-(3-Cl-pyridinyl)	225-226
783	*i*-Pr	H	2,4-di-F	Cl	2-(3-Cl-pyridinyl)	201-202
784	H	H	2,4-di-F	Cl	2-(3-Cl-pyridinyl)	128-129
785	Et	H	2-Me-4-Cl	CF_3	5-(1-CH_2CF_3-pyrazolyl)	172-174
786	Me	H	2-Me-4-Cl	CF_3	5-(1- CH_2CF_3-pyrazolyl)	192-194
787	Me	H	2,4-di-Cl	F	2-(3-Cl-pyridinyl)	*
788	Me	H	2-F	OCH_2CF_3	2-(3-Cl-pyridinyl)	202-203
789	Me	Me	2-F	OCH_2CF_3	2-(3-Cl-pyridinyl)	178-179

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
790	*i*-Pr	H	2-F	OCH_2CF_3	2-(3-Cl-pyridinyl)	161-162
791	Me	H	2-F-4-Br	Br	2-(3-Cl-pyridinyl)	209-210
792	Me	Me	2-F-4-Br	Br	2-(3-Cl-pyridinyl)	225-226
793	*i*-Pr	H	2-F-4-Br	Br	2-(3-Cl-pyridinyl)	208-209
794	Me	H	2-F-4-Br	Cl	2-(3-Cl-pyridinyl)	209-210
795	Me	Me	2-F-4-Br	Cl	2-(3-Cl-pyridinyl)	244-245
796	Me	Me	2-F-4-Br	Cl	2-(3-Cl-pyridinyl)	207-208
797	Me	H	2-F-4-Br	OCH_2CF_3	2-(3-Cl-pyridinyl)	210-211
798	Me	Me	2-F-4-Br	OCH_2CF_3	2-(3-Cl-pyridinyl)	204-206
799	*i*-Pr	H	2,4-di-Cl	CF_3	3-(4-Cl-5-Me-isoxazolyl)	204-205
800	Me	H	2,4-di-Cl	CF_3	3-(4-Cl-5-Me-isoxazolyl)	131-132
801	*i*-Pr	H	2-Me-4-Cl	CF_3	3-(4-Cl-5-Me-isoxazolyl)	188-189
802	Me	H	2-Me-4-Cl	CF_3	3-(4-Cl-5-Me-isoxazolyl)	210-211
803	*i*-Pr	H	2,4-di-Cl	CF_3	3-(4-Cl-isoxazolyl)	212-213
804	*i*-Pr	H	2-Me-4-Cl	CF_3	3-(4-Cl-isoxazolyl)	232
805	Me	H	2-Me-4-Cl	CF_3	3-(4-Cl-isoxazolyl)	190-191
806	Me	H	2,4-di-Cl	CF_3	3-(4-Cl-isoxazolyl)	209-210
807	*i*-Pr	H	4-Cl	CF_3	3-(4-Cl-isoxazolyl)	241-242
808	*i*-Pr	H	2,4-di-Cl	CF_3	5-(1-CH_2CF_3-pyrazolyl)	212-214
809	H	H	2,4-di-Cl	F	2-(3-Cl-pyridinyl)	*
810	*i*-Pr	H	2,4-di-Cl	F	2-(3-Cl-pyridinyl)	*
811	Me	Me	2,4-di-Cl	F	2-(3-Cl-pyridinyl)	*
812	H	H	2-Me-4-Cl	F	2-(3-Cl-pyridinyl)	*
813	*i*-Pr	H	2-Me-4-Cl	F	2-(3-Cl-pyridinyl)	*
814	Me	H	2-Me-4-Cl	F	2-(3-Cl-pyridinyl)	*
815	Me	Me	2-Me-4-Cl	F	2-(3-Cl-pyridinyl)	*
816	Me	H	2,4-di-Cl	CF_3	5-(1-Me-4-Cl-pyrazolyl)	242-244
817	Et	H	2,4-di-Cl	CF_3	5-(1-Me-4-Cl-pyrazolyl)	266-268
818	*i*-Pr	H	2,4-di-Cl	CF_3	5-(1-Me-4-Cl-pyrazolyl)	241-243
819	Me	Me	2,4-di-Cl	CF_3	5-(1-Me-4-Cl-pyrazolyl)	202-204
820	*t*-Bu	H	2,4-di-Cl	CF_3	5-(1-Me-4-Cl-pyrazolyl)	128-131
821	Me	H	2,4-di-Cl	CF_3	2-(3-Cl-pyridinyl)	*
822	H	H	2-F-4-Br	Br	2-(3-Cl-pyridinyl)	151-152
823	H	H	2-Cl-4-F	Cl	2-(3-Cl-pyridinyl)	133-134
824	Me	H	2,4-di-F	F	2-(3-Cl-pyridinyl)	166-167
825	H	H	2-F-4-Br	Cl	2-(3-Cl-pyridinyl)	148-149
826	H	H	2-Br-4-Cl	Br	2-(3-Cl-pyridinyl)	134-136

Compound	R^3	R^2	R^4, R^5	R^6	R^7	m.p. (°C)
827	Me	Me	2,4-di-F	F	2-(3-Cl-pyridinyl)	211-212
828	H	H	2,4-di-F	F	2-(3-Cl-pyridinyl)	115-117
829	*i*-Pr	H	2,4-di-F	F	2-(3-Cl-pyridinyl)	157-158
830	*i*-Pr	H	2-Cl-4-I	Cl	2-(3-Cl-pyridinyl)	192-195
831	*i*-Pr	H	2,4-di-Cl	OCH_3	2-(3-Cl-pyridinyl)	191-194
832	Me	H	2,4-di-Cl	OCH_3	2-(3-Cl-pyridinyl)	143-145
833	Me	H	2-Me-4-Cl	Br	2-(3-Cl-5-Br-pyridinyl)	216-219
834	Me	H	2-F	F	2-(3-Cl-pyridinyl)	217-218
835	Me	H	2-Cl-4-F	F	2-(3-Cl-pyridinyl)	207-208
836	Me	Me	2-Cl-4-F	F	2-(3-Cl-pyridinyl)	221-222
837	*i*-Pr	H	2-C-4-F	F	2-(3-Cl-pyridinyl)	166-167
838	H	H	2-Cl-4-F	F	2-(3-Cl-pyridinyl)	133-134
839	Me	H	2-F-4-I	Br	2-(3-Cl-pyridinyl)	216-217
840	Me	Me	2-F-4-I	Br	2-(3-Cl-pyridinyl)	218-219
841	*i*-Pr	H	2-F-4-I	Br	2-(3-Cl-pyridinyl)	217-218
842	H	H	2,4-di-F	Br	2-(3-Cl-pyridinyl)	178-179
843	Me	H	2-I-4-F	F	2-(3-Cl-pyridinyl)	217-218
844	Me	Me	2-I-4-F	F	2-(3-Cl-pyridinyl)	238-239
845	H	H	2-Me-4-Cl	CF_3	2-(3-F-pyridinyl)	*
846	Me	H	2-Me-4-Cl	CF_3	2-(3-F-pyridinyl)	*
847	Me	Me	2-Me-4-Cl	CF_3	2-(3-F-pyridinyl)	*
848	*i*-Pr	H	2-Me-4-Cl	CF_3	2-(3-F-pyridinyl)	*
849	H	H	2,4-di-Cl	CF_3	2-(3-F-pyridinyl)	*
850	Me	Me	2,4-di-Cl	CF_3	2-(3-F-pyridinyl)	*
851	*i*-Pr	H	2,4-di-Cl	CF_3	2-(3-F-pyridinyl)	*
852	H	H	2,4-di-Cl	Br	2-(3-F-pyridinyl)	*
853	Me	H	2,4-di-Cl	Br	2-(3-F-pyridinyl)	*
854	Me	Me	2,4-di-Cl	Br	2-(3-F-pyridinyl)	*
855	*i*-Pr	H	2,4-di-Cl	Br	2-(3-F-pyridinyl)	*
856	H	H	2-Me-4-Cl	Br	2-(3-F-pyridinyl)	*
857	Me	H	2-Me-4-Cl	Br	2-(3-F-pyridinyl)	*
858	Me	Me	2-Me-4-Cl	Br	2-(3-F-pyridinyl)	*
859	*i*-Pr	H	2-Me-4-Cl	Br	2-(3-F-pyridinyl)	*
860	Me	H	2,4-di-Cl	CF_3	5-(1-CH_2CF_3-4-Cl-pyrazolyl)	181-183

*See Index Table B for ^1H NMR data

INDEX TABLE B

Compound	^1H NMR Data ($CDCl_3$ solution unless indicated otherwise)[a]
191	(DMSO-d_6) δ 1.03 (d, 6H), 2.18 (s, 3H), 3.92 (m, 1H), 7.22-7.30 (m, 2H), 7.35 (m, 1H), 7.62 (dd, 1H), 7.81 (s, 1H), 8.02 (d, 1H), 8.15 (dd, 1H), 8.55 (dd, 1H), 10.34 (s, 1H).
224	(DMSO-d_6) δ 1.01 (d, 6H), 2.16 (s, 3H), 3.92 (m, 1H), 7.27 (m, 2H), 7.35 (m, 1H), 7.89 (s, 1H), 7.96 (m, 1H), 8.37 (s, 2H), 10.42 (s, 1H).
248	(DMSO-d_6) δ 1.04 (d, 6H), 4.0 (m, 1H), 7.4 (m, 2H), 7.5 (m, 1H), 7.6 (m 1H), 7.78 (d, 2H), 8.0 (d, 2H), 8.2 (d, 1H), 10.7 (bs, 1H).
249	(DMSO-d_6) δ 1.16 (d, 6H), 4.1 (m, 1H), 5.9 (d, 1H), 7.1 (m, 1H), 7.2 (m, 3H), 7.69 (s, 1H), 7.73 (s, 1H), 10.45 (s, 1H).
250	(DMSO-d_6) δ 1.0(d, 6H), 3.9 (m, 1H), 7.4 (m, 2H), 7.6 (m, 1H), 7.8 (m, 2H), 8.0 (d, 1H), 8.1 (d, 1H), 8.3 (s, 1H), 10.6 (s, 1H).
251	(DMSO-d_6) δ 1.0 (d, 6H), 4.0 (m, 1H), 7.1 (m, 1H), 7.43 (m, 2H), 7.5 (m, 4H), 7.66 (m, 2H), 10.6 (s, 1H).
254	(DMSO-d_6) δ 1.02 (d, 6H), 2.18 (s, 3H), 3.9-4.0 (m, 1H), 7.2 (m, 1H), 7.4 (m, 1H), 7.8-7.9 (m, 2H), 8.0 (d, 2H), 8.3 (s, 1H), 10.3 (s, 1H).
255	(DMSO-d_6) δ 1.02 (d, 6H), 2.18 (s, 3H), 3.9-4.0 (m, 1H), 7.2 (m, 1H), 7.4 (m, 1H), 7.8-7.9 (m, 2H), 8.0 (d, 2H), 8.3 (s, 1H), 10.3 (s, 1H).
256	(DMSO-d_6) δ 1.04 (d, 6H), 4.0 (m, 1H), 7.4 (m, 2H), 7.76 (s, 1H), 7.7 (m, 1H), 7.74 (m, 1H), 7.9 (m, 1H), 7.97 (d, 1H), 8.07 (s, 1H), 8.2 (m, 1H), 10.7 (bs, 1H).
271	(DMSO-d_6) δ 1.0 (d, 6H), 2.01 (s, 3H), 2.17 (s, 3H), 3.9 (m, 1H), 7.3 (m, 2H), 7.3-7.4 (m, 1H), 7.8-7.9 (s, 1H), 7.9-8.0 (m, 2H), 8.1-8.2 (s, 1H), 10.3-10.4 (s, 1H).
280	(DMSO-d_6) δ 1.21 (d, 6H), 2.24 (s, 3H), 4.1-4.3 (m, 1H), 5.9 (d, 1H), 7.02 (d, 1H), 7.1-7.6 (m, 7H), 7.78 (s, 1H), 10.0 (br s, 1H).
281	(DMSO-d_6) δ 1.03 (d, 6H), 1.94 (s, 3H), 2.14 (s, 3H), 3.9-4.0 (m, 1H), 7.1-7.4 (m, 8H), 7.8 (s, 1H), 7.9-8.0 (d, 1H), 10.0 (s, 1H).
282	(DMSO-d_6) δ 1.04 (d, 6H), 2.18 (s, 3H), 3.9-4.0 (m, 1H), 7.2-7.4 (m, 6H), 7.4-7.6 (m, 2H), 7.9 (s, 1H), 7.9-8.0 (d, 1H), 10.1 (br s, 1H).
285	δ 1.20 (d, 6H), 2.19 (s, 3H), 4.2 (m, 1H), 5.9-6.0 (d, 1H), 7.1-7.5 (m, 8H), 10.4-10.5 (s, 1H).
321	(DMSO-d_6) δ 1.03 (d, 6H), 2.18 (s, 3H), 3.31 (s, 3H), 3.9-4.0 (m, 1H), 7.2-7.3 (m, 2H), 7.3-7.4 (m, 1H), 7.81 (s, 1H), 7.9 (d, 1H), 8.0 (br d, 1H), 8.1 (dd, 1H), 8.3 (d, 1H), 10.3 (s, 1H).
405	δ 2.57 (t, 2H), 3.57 (q, 2H), 6.25 (t, 1H), 7.18-7.53 (m, 8H), 9.17 (s, 1H)

Compound	^1H NMR Data ($CDCl_3$ solution unless indicated otherwise)[a]
406	δ 1.23 (d, 6H), 4.13 (m, 1H), 5.92 (d, 1H), 7.35 (m, 1H), 7.39 (s, 1H) 7.42 (m, 2H), 7.92 (d, 1H), 8.51 (d, 1H), 10.23 (br s, 1H).
409	δ 1.13 (d, 6H), 4.15 (m, 1H), 5.99 (d, 1H), 7.40 (m, 1H), 7.41 (m, 1H), 7.63 (m, 1H), 7.80 (s, 1H), 7.90 (d, 1H), 8.48 (d, 1H), 10.2 (br s, 1H).
495	δ 1.22 (d, 6H), 2.18 (s, 3H), 4.15 (m, 1H), 4.37 (s, 1H), 5.91 (d, 1H), 7.20 (m, 4H), 7.30 (m, 1H), 7.40 (m, 1H), 7.52 (m, 2H), 7.96 (s, 1H), 10.23 (s, 1H).
496	(DMSO- d_6) δ 1.05 (d, 6H), 2.15 (s, 3H), 3.74 (s, 2H), 3.93 (m, 1H), 7.26-7.70 (m, 8H), 8.05 (s, 1H), 8.35 (br s, 2H), 10.45 (s, 1H).
511	δ 1.20 (d, 6H), 2.01 (s, 3H), 2.72 (d, 3H), 4.13 (m, 1H), 6.01 (d, 1H), 6.45 (s, 1H), 7.17 (m, 5H), 7.51 (m, 2H), 7.63 (m, 1H), 10.41 (s, 1H).
593	(DMSO- d_6) δ 1.04 (d, 6H), 2.32 (s, 3H), 3.91 (m, 1H), 7.44-7.64 (m, 4H), 7.77 (s, 1H), 8.07 (d, 1H), 8.27 (d, 1H), 8.42 (d, 1H), 10.6 (s, 1H).
597	(DMSO- d_6) δ 1.03 (d, 6H), 3.88 (m, 1H), 7.65 (dd, 1H), 7.88 (s, 1H), 8.18 (s, 1H), 8.22 (d, 1H), 8.48-8.57 (m, 3H), 10.95 (s, 1H).
599	δ 1.24 (d, 6H), 4.22 (m, 1H), 5.98 (br d, 1H), 7.30-7.55 (m, 6H), 7.78 (d, 1H), 7.99 (d, 1H), 11.15 (s, 1H).
645	δ 1.30 (t, 3H), 2.32 (s, 3H), 3.55 (q, 2H), 6.23 (br t, 1H), 7.30 (s, 1H), 7.42 (dd, 1H), 7.91 (d, 1H), 8.20 (apparent s, 2H), 8.52 (d, 1H), 10.92 (s, 1H).
646	δ 2.21 (s, 3H), 2.90 (s, 3H), 3.12 (s, 3H), 7.42 (m, 2H), 7.92 (d, 1H), 7.92 (d, 1H), 8.00 (d, 1H), 8.50 (d, 1H), 9.92 (br s, 1H).
647	δ 2.32 (s, 3H), 4.02 (t, 2H), 5.18-5.30 (m, 2H), 5.82-5.98 (m, 1H), 7.37 (s, 1H), 7.43 (dd, 1H), 7.50 (br t, 1H), 7.92 (d, 1H), 8.17 (s, 1H), 8.37 (d, 1H), 8.52 (d, 1H), 11.12 (br s, 1H).
648	δ 0.91 (t, 3H), 1.63 (m, 2H), 2.31 (s, 3H), 3.40 (q, 2H), 6.83 (br t, 1H), 7.35 (s, 1H), 7.42 (dd, 1H), 7.91 (d, 1H), 8.17 (d, 1H), 8.24 (d, 1H), 8.52 (d, 1H), 11.03 (s, 1H).
649	δ 1.38 (d, 3H), 2.14 (s, 3H), 2.35 (s, 3H), 2.72 (m, 2H), 4.38 (m, 1H), 6.93 (br d, 1H), 7.33 (s, 1H), 7.43 (dd, 1H), 7.91 (d, 1H), 8.18 (d, 1H), 8.28 (d, 1H), 8.52 (d, 1H), 10.93 (s, 1H).
650	(DMSO- d_6) δ 2.32 (s, 3H), 2.70 (s, 3H), 7.63 (m, 2H), 7.78 (br s, 1H), 8.18 (br s, 1H), 8.21 (d, 1H), 8.27 (br s, 1H), 8.58 (m, 2H).
651	(DMSO- d_6) δ 1.25 (s, 9H), 2.31 (s, 3H), 7.64 (dd, 1H), 7.79 (s, 1H), 8.03 (br s, 2H), 8.22 (d, 1H), 8.28 (s, 1H), 8.54 (d, 1H), 10.62 (s, 1H).
661	δ 2.33 (s, 3H), 2.75 (br s, 6H), 6.9 (br s, 1H), 7.33 (s, 1H), 7.43 (dd, 1H), 7.91 (d, 1H), 8.19 (br s, 1H), 8.23 (s, 1H), 8.50 (d, 1H), 10.70 (br s, 1H).
742	δ 1.39 (d, 6H), 2.81 (d, 3H), 4.95 (m, 1H), 6.59 (s, 1H), 6.62 (q, 1H), 7.12

Compound	^{1}H NMR Data ($CDCl_3$ solution unless indicated otherwise)[a]
	(s, 1H), 7.24 (s, 1H), 7.26 (t, 1H), 7.80 (d, 1H), 8.40 (d, 1H), 9.56 (br s, 1H).
779	δ 1.24 (d, 6H), 2.22 (s, 3H), 4.20 (m, 1H), 6.10 (d, 1H), 7.35 (s, 1H), 7.44 (t, 1H), 7.55 (s, 2H), 7.87 (s, 1H), 8.48 (d, 1H), 10.7 (s, 1H).
787	δ 2.91 (d, 3H), 6.3 (m, 1H), 6.77 (d, 1H), 7.3 (obscured, 1H), 7.3-7.4 (m, 2H), 7.8-7.9 (d, 1H), 8.5 (d, 1H), 9.6-9.7 (br s, 1H).
809	(DMSO- d_6) δ 7.1 (d, 1H), 7.5-7.7 (m, 3H), 7.8 (m, 2H), 8.1-8.2 (d, 1H), 8.5 (d, 1H), 10.5 (br s, 1H).
810	(DMSO- d_6) δ 1.03 (d, 6H), 3.9 (m, 1H), 7.1 (d, 1H), 7.4-7.5 (d, 1H), 7.6 (dd, 1H), 7.8 (d, 1H), 8.2 (d, 1H), 8.2 (m, 1H), 8.5 (d, 1H), 10.5 (br s, 1H).
811	δ 2.78 (s, 3H), 3.04 (s, 3H), 6.9 (d, 1H), 7.1 (d, 1H), 7.29 (d, 1H), 7.3-7.4 (dd, 1H), 7.8-7.9 (d, 1H), 8.5 (d, 1H), 9.8 (br s, 1H).
812	δ 2.18 (s, 3H), 5.7 (br s, 1H), 6.2 (br s, 1H), 6.7 (d, 1H), 7.3 (m, 1H), 7.3-7.4 (dd, 1H), 7.8-7.9 (d, 1H), 8.4-8.5 (d, 1H), 10.0 (br s, 1H).
813	δ 1.23 (d, 6H), 2.19 (s, 3H), 4.2 (m, 1H), 5.9 (br s, 1H), 6.7 (d, 1H), 7.21 (d, 1H), 7.26 (obscured, 1H), 7.3-7.4 (dd, 1H), 7.8-7.9 (d, 1H), 8.4-8.5 (d, 1H), 10.1 (br s, 1H).
814	δ 2.20 (s, 3H), 2.96 (d, 3H), 6.1 (br s, 1H), 6.65 (d, 1H), 7.2 (d, 1H), 7.26 (obscured, 1H), 7.3-7.4 (dd, 1H), 7.8-7.9 (d, 1H), 8.4-8.5 (d, 1H), 10.1 (br s, 1H).
815	δ 2.06 (s, 3H), 2.78 (s, 3H), 3.08 (s, 3H), 6.9 (d, 1H), 7.0 (s, 1H), 7.1 (s, 1H), 7.3-7.4 (dd, 1H), 7.8-7.9 (d, 1H), 8.4-8.5 (d, 1H), 9.7-9.8 (br s, 1H).
821	(DMSO- d_6) δ 2.65 (d, 3H), 7.52 (d, 1H), 7.6-7.8 (m, 2H), 7.9 (d, 1H), 8.0-8.1 (t, 1H), 8.3-8.4 (m, 1H), 8.4 (d, 1H), 10.7 (br s, 1H).
845	(DMSO- d_6) δ 2.18 (s, 3H), 7.41 (d, 1H), 7.5 (m, 2H), 7.67 (s, 1H), 7.7 (m, 1H); 7.8 (s, 1H), 8.0-8.1 (t, 1H), 8.4 (d, 1H), 10.4-10.5 (br s, 1H).
846	(DMSO- d_6) δ 2.18 (s, 3H), 2.66 (d, 3H), 7.35 (d, 1H), 7.49 (d, 1H), 7.69 (s, 1H), 7.7-7.8 (m, 1H), 8.0-8.1 (t, 1H), 8.3 (m, 1H), 8.4 (d, 1H), 10.4-10.5 (br s, 1H).
847	δ 2.00 (s, 3H), 2.75 (s, 3H), 3.09 (s,3H), 6.99 (d, 1H), 7.03 (s, 1H), 7.4-7.5 (m, 1H), 7.5-7.6 (t, 1H), 7.76 (d, 1H), 8.4 (d, 1H), 10.4-10.5 (br s, 1H).
848	(DMSO- d_6) δ 1.02 (d, 6H), 2.19 (s, 3H), 3.9 (m, 1H), 7.30 (s, 1H), 7.48 (d, 1H), 7.6-7.8 (m, 2H), 8.0 (t, 1H), 8.1 (d, 1H), 8.4 (d, 1H), 10.4 (br s, 1H).
849	(DMSO- d_6) δ 7.56 (d, 1H), 7.6 (s, 1H), 7.7-7.8 (m, 2H), 7.9 (m, 2H), 8.0-8.1 (t, 1H), 8.4 (d, 1H), 10.6-10.7 (br s, 1H).
850	δ 2.79 (s, 3H), 3.08 (s, 3H), 7.09 (d, 1H), 7.25 (d, 1H), 7.4-7.5 (m, 1H),

Compound	^{1}H NMR Data ($CDCl_3$ solution unless indicated otherwise)[a]
	7.5-7.6 (t, 1H), 7.78 (s, 1H), 8.4 (d, 1H), 10.5 (br s, 1H).
851	(DMSO- d_6) δ 1.01 (d, 6H), 3.9 (m, 1H), 7.46 (d, 1H), 7.7 (m, 1H), 7.8 (s, 1H), 7.85 (d, 1H), 8.0 (t, 1H), 8.2-8.3 (d, 1H), 8.4 (d, 1H), 10.6-10.7 (br s, 1H).
852	(DMSO- d_6) δ 7.39 (s, 1H), 7.55 (d, 1H), 7.4 (s, 1H), 7.4-7.5 (m, 1H), 7.8 (s, 1H), 7.85 (d, 1H), 8.0 (t, 1H), 8.4 (d, 1H), 10.5 (br s, 1H).
853	(DMSO- d_6) δ 2.66 (d, 3H), 7.40 (s, 1H), 7.51 (d, 1H), 7.6-7.7 (m, 1H), 7.84 (d, 1H), 8.0 (t, 1H), 8.3-8.4 (m, 1H), 8.4 (d, 1H), 10.5-10.6 (br s, 1H).
854	δ 2.80 (s, 3H), 3.07 (s, 3H), 7.10 (s, 1H), 7.31 (d, 1H), 7.35 (s, 1H), 7.4 (m, 1H), 7.5-7.6 (t, 1H), 8.4 (d, 1H), 9.5 (br s, 1H).
855	(DMSO- d_6) δ 1.02 (d, 6H), 3.9 (m, 1H), 7.45 (apparent s, 2H), 7.6-7.7 (m, 1H), 7.84 (d, 1H), 7.9-8.0 (t, 1H), 8.2 (d, 1H), 8.36 (d, 1H), 10.5 (br s, 1H).
856	(DMSO- d_6) δ 2.17 (s, 3H), 7.33 (s, 1H), 7.4 (d, 1H), 7.5 (m, 2H), 7.6-7.7 (m, 1H), 7.9 (s, 1H), 8.0 (t, 1H), 8.4 (d, 1H), 10.3 (br s, 1H).
857	(DMSO- d_6) δ 2.17 (s, 3H), 2.67 (d, 3H), 7.3-7.4 (m, 2H), 7.5 (d, 1H), 7.6-7.7 (m, 1H), 8.0 (t, 1H), 8.2-8.3 (m, 1H), 8.4 (d, 1H), 10.3 (br s, 1H).
858	δ 2.08 (s, 3H), 2.79 (s, 3H), 3.09 (s, 3H), 6.99 (d, 1H), 7.11 (s, 1H), 7.28 (d, 1H), 7.4 (m, 1H), 7.5-7.6 (t, 1H), 8.3-8.4 (d, 1H), 9.8 (br s, 1H).
859	(DMSO- d_6) δ 1.03 (d, 6H), 2.17 (s, 3H), 3.9 (m, 1H), 7.3 (d, 1H), 7.37 (s, 1H), 7.5 (d, 1H), 7.6-7.7 (m, 1H), 7.9-8.0 (t, 1H), 8.1 (d, 1H), 8.3-8.4 (d, 1H), 10.2-10.3 (br s, 1H).

[a] ^{1}H NMR data are in ppm downfield from tetramethylsilane. Couplings are designated by (s)-singlet, (d)-doublet, (t)-triplet, (q)-quartet, (m)-multiplet, (dd)-doublet of doublets, (dt)-doublet of triplets, (br s)-broad singlet.

BIOLOGICAL EXAMPLES OF THE INVENTION

TEST A

For evaluating control of fall armyworm (*Spodoptera frugiperda*) the test unit consisted of a small open container with a 4–5-day-old corn (maize) plant inside. This was pre-infested with 10–15 1-day-old larvae on a piece of insect diet by use of a core sampler to remove a plug from a sheet of hardened insect diet having many larvae growing on it and transfer the plug containing larvae and diet to the test unit. The larvae moved onto the test plant as the diet plug dried out.

Test compounds were formulated using a solution containing 10% acetone, 90% water and 300 ppm X-77® Spreader Lo-Foam Formula non-ionic surfactant containing alkylarylpolyoxyethylene, free fatty acids, glycols and isopropanol (Loveland Industries, Inc.), unless otherwise indicated. The formulated compounds were applied in 1 mL of liquid

through a SUJ2 atomizer nozzle with 1/8 JJ custom body (Spraying Systems Co.) positioned 1.27 cm (0.5 inches) above the top of each test unit. All experimental compounds in this screen were sprayed at 50 ppm and replicated three times. After spraying of the formulated test compound, each test unit was allowed to dry for 1 hour and then a black, screened cap was placed on top. The test units were held for 6 days in a growth chamber at 25 °C and 70% relative humidity. Plant feeding damage was then visually assessed.

Of the compounds tested, the following provided excellent levels of plant protection (10% or less feeding damage): 5, 11, 18, 19, 24, 28, 30, 32, 33, 34, 37, 38, 39, 40, 45, 46, 47, 48, 56, 57, 58, 59, 63, 64, 75, 76, 77, 78, 79, 84, 85, 86, 87, 91, 93, 94, 95, 96, 97, 98, 99, 108, 113, 114, 116, 115, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 133, 135, 136, 141, 142, 143, 144, 145, 147, 148, 149, 150, 151, 153, 154, 155, 156, 157, 158, 160, 161, 164, 165, 166, 168, 169, 170, 174, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 207, 208, 209, 210, 211, 212, 213, 214, 218, 219, 220, 221, 222, 224, 229, 230, 231, 232, 233, 234, 236, 237, 238, 244, 246, 247, 250, 257, 258, 259, 267, 268, 270, 271, 272, 273, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 287, 288, 289, 290, 291, 292, 293, 294, 295, 297, 298, 299, 300, 301, 302, 305, 306, 307, 309, 313, 314, 315, 316, 319, 320, 321, 322, 324, 325, 326, 327, 328, 329, 330, 335, 336, 338, 339, 341, 344, 345, 346, 347, 348, 349, 351, 352, 356, 364, 365, 366, 367, 370, 371, 372, 373, 374, 376, 377, 384, 387, 388, 390, 391, 392, 393, 394, 395, 396, 401, 402, 404, 405, 406, 407, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 426, 428, 429, 430, 431, 432, 433, 434, 446, 449, 453, 454, 456, 457, 458, 459, 460, 461, 462, 463, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 481, 482, 483, 484, 486, 487, 488, 489, 494, 497, 499, 500, 501, 502, 505, 506, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 611, 612, 613, 615, 616, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 647, 648, 649, 650, 651, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 713, 714, 715, 716, 717, 718, 719, 720, 721, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 759, 762, 763, 766, 767, 768, 769, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 787, 790, 791, 792, 793, 794, 795, 796, 797, 798, 801,

804, 809, 810, 811, 812, 813, 814, 815, 816, 817, 818, 820, 821, 822, 823, 824, 825, 826, 829, 830, 831, 832 and 833.

TEST B

For evaluating control of tobacco budworm (*Heliothis virescens*) the test unit consisted of a small open container with a 6–7 day old cotton plant inside. This was pre-infested with 8 2-day-old larvae on a piece of insect diet by use of a core sampler as described for Test A.

Test compounds were formulated and sprayed at 50 ppm as described for Test A. The applications were replicated three times. After spraying, the test units were maintained in a growth chamber and then visually rated as described for Test A.

Of the compounds tested, the following provided excellent levels of plant protection (10% or less feeding damage): 8, 11, 18, 24, 28, 30, 32, 33, 34, 37, 39, 46, 47, 48, 53, 56, 57, 58, 59, 60, 74, 75, 76, 77, 78, 79, 80, 82, 84, 85, 86, 87, 88, 91, 93, 94, 95, 96, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 141, 142, 143, 145, 147, 150, 151, 153, 154, 155, 156, 158, 160, 161, 164, 165, 166, 168, 169, 170, 171, 174, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 207, 208, 209, 210, 211, 212, 213, 214, 216, 218, 219, 220, 221, 222, 223, 224, 229, 230, 231, 232, 233, 234, 236, 237, 238, 239, 240, 244, 246, 247, 250, 257, 258, 267, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 304, 305, 306, 307, 309, 313, 314, 315, 316, 319, 320, 321, 322, 324, 325, 326, 327, 328, 336, 338, 339, 341, 345, 346, 348, 353, 356, 357, 364, 366, 367, 370, 371, 372, 373, 374, 377, 381, 383, 384, 385, 387, 388, 390, 391, 392, 393, 394, 395, 397, 399, 401, 402, 404, 405, 406, 407, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 428, 429, 430, 431, 432, 433, 434, 444, 445, 446, 447, 449, 453, 454, 456, 457, 458, 459, 460, 461, 462, 468, 469, 470, 471, 472, 474, 473, 475, 476, 477, 478, 479, 481, 482, 483, 484, 486, 487, 488, 489, 494, 497, 499, 500, 501, 502, 506, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 600, 601, 602, 603, 605, 608, 609, 611, 612, 613, 614, 615, 616, 619, 620, 621, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 647, 648, 649, 650, 651, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 713, 714, 715, 716, 717, 718, 719, 720, 721, 724, 725, 726, 727, 728, 729, 730,

731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 742, 743, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754 and 755.

TEST C

For evaluating control of beet armyworm (*Spodoptera exigua*) the test unit consisted of a small open container with a 4–5-day-old corn (maize) plant inside. This was pre-infested with 10–15 1-day-old larvae on a piece of insect diet by use of a core sampler as described for Test A.

Test compounds were formulated and sprayed at 50 ppm as described for Test A. The applications were replicated three times. After spraying, the test units were maintained in a growth chamber and then visually rated as described for Test A.

Of the compounds tested, the following provided excellent levels of plant protection (10% or less feeding damage): 5, 8, 11, 18, 19, 24, 28, 30, 32, 33, 34, 37, 38, 39, 46, 47, 48, 53, 56, 57, 58, 59, 60, 63, 64, 74, 75, 76, 77, 78, 79, 84, 85, 86, 87, 88, 91, 92, 93, 94, 95, 96, 97, 98, 99, 101, 102, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 133, 135, 136, 137, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 153, 154, 155, 156, 157, 158, 160, 161, 164, 165, 166, 168, 169, 170, 174, 176, 177, 178, 179, 180, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 195, 196, 197, 198, 199, 201, 202, 207, 208, 209, 210, 211, 212, 214, 218, 219, 221, 224, 229, 230, 231, 232, 233, 234, 236, 237, 238, 239, 240, 244, 246, 247, 250, 257, 258, 267, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 297, 298, 299, 300, 301, 302, 304, 305, 307, 309, 313, 314, 315, 316, 319, 320, 321, 322, 324, 325, 326, 327, 328, 330, 336, 338, 339, 341, 343, 344, 345, 346, 347, 348, 351, 352, 356, 364, 365, 366, 367, 370, 371, 372, 373, 374, 376, 377, 380, 384, 385, 387, 388, 389, 390, 391, 392, 393, 394, 395, 401, 402, 404, 405, 406, 407, 409, 410, 413, 414, 418, 420, 422, 423, 424, 428, 429, 430, 431, 432, 433, 434, 449, 453, 454, 456, 457, 458, 459, 460, 461, 462, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 481, 482, 483, 484, 486, 487, 488, 494, 497, 499, 500, 501, 502, 506, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 595, 596, 597, 598, 600, 601, 603, 605, 606, 607, 608, 609, 611, 612, 613, 614, 616, 619, 620, 621, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 647, 648, 650, 651, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 669, 671, 672, 673, 674, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 713, 714, 715, 719, 720,

721, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754 and 755.

TEST D

For evaluating control of green peach aphid (*Myzus persicae*) through contact and/or systemic means, the test unit consisted of a small open container with a 12–15-day-old radish plant inside. This was pre-infested by placing on a leaf of the test plant 30–40 insects on a piece of leaf excised from a culture plant (cut-leaf method). The larvae moved onto the test plant as the leaf piece desiccated. After pre-infestation, the soil of the test unit was covered with a layer of sand.

Test compounds were formulated using a solution containing 10% acetone, 90% water and 300 ppm X-77® Spreader Lo-Foam Formula non-ionic surfactant containing alkylarylpolyoxyethylene, free fatty acids, glycols and isopropanol (Loveland Industries, Inc.), unless otherwise indicated. The formulated compounds were applied in 1 mL of liquid through a SUJ2 atomizer nozzle with 1/8 JJ custom body (Spraying Systems Co.) positioned 1.27 cm (0.5 inches) above the top of each test unit. All experimental compounds in this screen were sprayed at 250 ppm and replicated three times. After spraying of the formulated test compound, each test unit was allowed to dry for 1 hour and then a black, screened cap was placed on top. The test units were held for 6 days in a growth chamber at 19–21 °C and 50–70% relative humidity. Each test unit was then visually assessed for insect mortality.

Of the compounds tested, the following resulted in at least 80% mortality: 283, 297, 370, 371, 372, 388, 431, 434, 469, 470, 472, 473, 474, 476, 479, 486, 494, 497, 499, 500, 501, 502, 506, 512, 514, 515, 516, 517, 518, 520, 530, 531, 532, 533, 534, 536, 537, 538, 539, 540, 542, 543, 544, 546, 548, 549, 550, 551, 553, 554, 555, 557, 559, 560, 561, 562, 563, 564, 565, 566, 567, 569, 571, 575, 576, 577, 578, 579, 580, 582, 584, 590, 596, 597, 601, 602, 603, 604, 609, 611, 614, 619, 620, 621, 624, 625, 626, 627, 629, 630, 631, 633, 638, 639, 640, 641, 642, 643, 644, 645, 650, 651, 655, 656, 657, 661, 664, 669, 671, 672, 673, 674, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 691, 698, 699, 703, 708, 709, 710, 711, 719, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 771, 776, 779, 780, 781, 783, 784, 787, 793, 809, 810, 811, 812, 821, 822, 823, 824, 825, 826, 830, 831, 832 and 833.

TEST E

For evaluating control of cotton melon aphid (*Aphis gossypii*) through contact and/or systemic means, the test unit consisted of a small open container with a 6–7-day-old cotton plant inside. This was pre-infested with 30–40 insects on a piece of leaf according to the cut-leaf method described for Test D, and the soil of the test unit was covered with a layer of sand.

Test compounds were formulated and sprayed at 250 ppm as described for Test D. The applications were replicated three times. After spraying, the test units were maintained in a growth chamber and then visually rated as described for Test D.

Of the compounds tested, the following resulted in at least 80% mortality: 370, 371, 372, 388, 431, 470, 472, 474, 476, 486, 494, 497, 500, 501, 506, 512, 514, 515, 516, 517, 518, 520, 530, 531, 532, 533, 534, 536, 537, 538, 539, 540, 542, 543, 544, 546, 548, 549, 550, 551, 553, 554, 555, 557, 559, 560, 561, 562, 563, 564, 566, 567, 568, 575, 576, 577, 578, 579, 582, 596, 601, 602, 603, 604, 609, 611, 620, 621, 624, 625, 626, 627, 628, 629, 630, 631, 638, 639, 640, 641, 642, 643, 644, 655, 656, 657, 661, 672, 673, 679, 681, 686, 687, 691, 698, 699, 703, 704, 706, 708, 709, 710, 711, 719, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 743, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 771, 774, 776, 777, 779, 780, 783, 784, 787, 791, 793, 794, 809, 811, 812, 821, 822, 823, 825 and 826.

TEST F

For evaluating control of corn planthopper (*Peregrinus maidis*) through contact and/or systemic means, the test unit consisted of a small open container with a 3-4 day old corn (maize) plant (spike) inside. White sand was added to the top of the soil prior to application. Test compounds were formulated and sprayed at 250 ppm and replicated three times as described for Test D. After spraying, the test units were allowed to dry for 1 hour before they were post-infested with 10-20 corn planthoppers (18 to 20 day old) nymphs) by sprinkling them onto the sand with a salt shaker. A black, screened cap was placed on the top of the cylinder. The test units were held for 6 days in a growth chamber at 19–21 °C and 50–70% relative humidity. Each test unit was then visually assessed for insect mortality.

Of the compounds tested, the following resulted in at least 80% mortality: 370, 371, 372, 388, 431, 469, 470, 472, 474, 476, 486, 489, 494, 497, 500, 501, 506, 512, 514, 515, 516, 517, 518, 520, 530, 531, 532, 533, 534, 536, 537, 538, 539, 540, 542, 543, 544, 546, 548, 549, 550, 551, 553, 554, 555, 557, 559, 560, 561, 562, 563, 564, 566, 567, 568, 575, 576, 577, 578, 579, 582, 596, 601, 602, 603, 604, 609, 611, 620, 621, 624, 625, 626, 627, 628, 629, 630, 631, 638, 639, 640, 641, 642, 643, 644, 655, 656, 657, 661, 672, 673, 679, 681, 686, 687, 691, 698, 699, 703, 704, 706, 708, 709, 710, 711, 719, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 743, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 771, 774, 776, 777, 779, 780, 781, 783, 784, 787, 791, 793, 794, 809, 811, 812, 814, 821, 822, 823, 825 and 826.

TEST G

For evaluating control of potato leafhopper (*Empoasca fabae* Harris) through contact and/or systemic means, the test unit consisted of a small open container with a 5-6 day old Longio bean plant (primary leaves emerged) inside. White sand was added to the top of the

soil and one of the primary leaves was excised prior to application. Test compounds were formulated and sprayed at 250 ppm and replicated three times as described for Test D. After spraying, the test units were allowed to dry for 1 hour before they were post-infested with 5 potato leafhoppers (18 to 21 day old) adults). A black, screened cap is placed on the top of the cylinder. The test units were held for 6 days in a growth chamber at 19–21 °C and 50–70% relative humidity. Each test unit was then visually assessed for insect mortality.

Of the compounds tested, the following resulted in at least 80% mortality: 200, 233, 236, 283, 313, 316, 324, 370, 371, 372, 434, 456, 457, 469, 470, 471, 472, 473, 474, 475, 476, 482, 486, 494, 497, 499, 500, 501, 502, 506, 512, 514, 515, 516, 517, 518, 519, 520, 530, 531, 533, 534, 536, 537, 538, 539, 542, 543, 544, 549, 550, 551, 553, 554, 555, 557, 558, 559, 560, 561, 562, 563, 564, 566, 567, 568, 575, 576, 577, 578, 579, 582, 584, 601, 603, 609, 611, 614, 619, 621, 625, 626, 629, 630, 631, 632, 633, 634, 639, 640, 641, 643, 644, 655, 656, 657, 662, 664, 672, 678, 679, 680, 681, 682, 683, 685, 686, 687, 703, 706, 708, 710, 719, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 766, 771, 776, 777, 779, 780, 781, 784, 787, 793, 794, 796, 809, 810, 811, 812, 814, 821, 822, 824, 825, 826, 828, 831, 832 and 833.

TEST H

For evaluating control of silverleaf whitefly (*Bemisia tabaci*), the test unit consisted of a 14–21-day-old cotton plant grown in Redi-earth® media (Scotts Co.) with at least two true leaves infested with 2nd and 3rd instar nymphs on the underside of the leaves.

Test compounds were formulated in no more than 2 mL of acetone and then diluted with water to 25–30 mL. The formulated compounds were applied using a flat fan air-assisted nozzle (Spraying Systems 122440) at 10 psi (69 kPa). Plants were sprayed to run-off on a turntable sprayer. All experimental compounds in this screen were sprayed at 250 ppm and replicated three times. After spraying of the test compound, the test units were held for 6 days in a growth chamber at 50–60% relative humidity and 28 °C daytime and 24 °C nighttime temperature. Then the leaves were removed and the dead and live nymphs were counted to calculate percent mortality.

Of the compounds tested, the following resulted in at least 80% mortality: 494, 497, 499, 500, 501, 502, 506, 512, 513, 514, 515, 516, 517, 518, 520, 523, 530, 531, 532, 533, 534, 535, 536, 537, 538, 540, 542, 543, 544, 549, 550, 551, 553, 554, 555, 557, 560, 575, 576, 577, 578, 579, 601, 620, 625, 629, 641, 673, 686, 691 and 703.

TEST I

For evaluating soil systemic control of tobacco budworm (*Heliothis virescens*), cotton plants were grown in sassafras soil in 15-cm pots in aluminum trays. When the plants reached square stage (bud formation on the plant) the plants were treated with the test compounds.

Test compounds were formulated in 0.25 mL of acetone and then diluted with water to provide solutions of 10 ppm. Ten mL of the treatment solutions was added to the pots weekly for four weeks, with four replicates of each treatment rate. One day after the second, third and fourth treatments, 35–50 first instar *Heliothis virescens* larvae were brushed on each plant with paintbrushes and placed on the terminal area, squares, and bolls. Five days after the last infestation with larvae the plants were rated for damage. Of the compounds tested, the following provided excellent levels of plant protection at 10 ppm (10% or less feeding damage) with excellent protection of squares and bolls including no or minimal sepal demage: 214, 283 and 520.

TEST J

Test H followed an alternative protocol for evaluating soil systemic control of tobacco budworm (*Heliothis virescens*). Cotton plants were grown in sassafras soil in 15-cm pots under greenhouse conditions. When the plants reached square stage (bud formation on the plant) the soil surface was treated with the test compounds.

Test compounds were formulated in 0.25 mL of acetone and then diluted with water. Ten mL of treatment solution containing 3 mg of compound was added to the soil surface of each pot. The plants were watered the next day and each day following as needed. At 1, 2 and 4 days after treatment, leaves were excised for evaluation. Two sets of leaves were selected from each plant: upper leaves at approximately second node from terminal and with area greater than 25 cm^2 and lower leaves at approximately third node from bottom and with area greater than 25 cm^2. The excised leaves were cut into 3 cm x 2 cm sections and placed into test trays made of high-impact styrene consisting of sixteen contiguous wells, each 6 cm wide, 4 cm long and 3 cm deep, with a clear plastic lid molded so that it locked into each well by friction. Solidified agar was placed into the bottom of each well to maintain moisture for plant material. One second instar tobacco budworm was placed into each well with plant material; wells were sealed and held at 25 °C and provided with 16 hours of light per day

Of the compounds tested, the following compounds provided excellent levels of mortality (greater than 70% mortality) on upper leaves excised at 4 days after treatment at the test rate: 497, 530 and 543.

TEST K

For evaluating soil systemic control of fall armyworm (*Spodoptera frugiperda*), corn (maize) plants (Pioneer #3394) were grown in small pots for 5 days until they were at least 4 cm tall and the first leaf was unfurling.

Test compounds were dissolved in 0.25 mL of acetone and diluted with water provide solutions of 1, 10, 50 and 200 ppm. One mL of the test solution was applied by pipette to the surface of the soil in each pot, with eight plants for each compound/rate. The pots were covered and held at 25 °C with 16 hours of light per day. The plants were watered the next

ay and each day following as needed. After 6 days, the plant matter above the first leaf was excised and cut into 3-cm lengths. Each test unit was a high-impact styrene tray (Supplier: Clearpack Company, 11610 Copenhagen Court, Franklin Park, IL 60131) consisting of sixteen contiguous wells each 6 cm wide, 4 cm long and 3 cm deep, with a clear plastic lid molded so that it locks into each well by friction. Solidified agar (2 to 4 mL) was placed onto the bottom of each well to maintain moisture in the wells during the test. Each 3-cm length of corn plant matter was placed into a tray such that the plant matter was contained within two wells. One second-instar fall armyworm (*Spodoptera frugiperda*) larva was placed in each well, the tray was covered and then the test units were held at at 25 °C with 16 hours of light per day. Mortality was observed after four days.

LC_{90} concentrations (test compound concentrations giving 90% kill of the larvae) were calculated based on probit analysis (log linear regression) using a general linearized model (GLIM) of the SAS statistical computer analysis product of SAS Institute (Cary, NC, U.S.A.). Of the compounds tested, the following provided excellent levels of mortality, with LC_{90} values of 10 ppm or less: 200, 202, 313, 494, 497, 500, 513, 515, 516, 518, 520, 531, 533, 535, 538, 542, 543 and 544.

TEST L

For evaluating soil systemic control of Colorado potato beetle (*Leptinotarsa decemlineata*), transplanted tomato plants were grown in 6-cm pots for 5 days until they were at the two true leaf stage.

Test compounds were dissolved in 0.25 mL of acetone and diluted with water provide solutions of 5 ppm. Five mL of the appropriate test solution was applied by pipette to the surface of the soil in each pot, followed by 5 mL of water, with eight plants for each compound/rate. The pots were covered and held at 25 °C with 16 hours of light per day. The plants were watered the next day and each day following as needed. After 4 days, one leaf from each plant was excised and placed into a well of a test tray as described in Test H. One 5-day old Colorado potato beetle (*Leptinotarsa decemlineata*) was placed in each well, the tray was covered and then the test units were held at at 25 °C with 16 hours of light per day. Mortality was observed after four days.

Of the compounds tested, the following provided excellent levels of mortality and feeding inhibition at 5 ppm: 214.

TEST M

For evaluating control of boll weevil (*Anthonomus g. grandis*), samples of the test compounds were dissolved in 1 mL of acetone. This solution was then diluted to 100 mL total volume using an aqueous 500 ppm solution of Ortho X-77™ surfactant. Serial dilutions were made to obtain 50 mL of 50 ppm concentration.

The diluted solutions of the test compounds were sprayed to run-off on three-week-old cotton plants. The plants were placed on a rotating turntable sprayer (10 rpm). Test solutions were applied using a flat fan air-assisted nozzle (Spraying Systems 122440) at 10 psi (69 kPa). Sprayed and dried plants were incased in a plastic cylinder. Twenty weevils were placed in each cylinder containing a whole cotton plant. At three days after infestation a feeding damage rating was taken.

Of the compounds tested, the following provided excellent levels of plant protection at 50 ppm (10% or less feeding damage): 530 and 531.

TEST N

For evaluating control of thrips (*Frankliniella sp.*), samples of the test compounds were dissolved in 1 mL of acetone. This solution was then diluted to 100 mL total volume using an aqueous 500 ppm solution of Ortho X-77™ surfactant. Serial dilutions were made to obtain 50 mL of 10 ppm concentration.

The diluted solutions of the test compounds were sprayed to run-off on three-week-old cotton or soybean plants infested with thrips. The plants were placed on a rotating turntable sprayer (10 rpm). Test solutions were applied using a flat fan air-assisted nozzle (Spraying Systems 122440) at 10 psi (69 kPa). Sprayed and dried plants were incased in a plastic cylinder. At four days after application the total number of dead thrips was recorded.

Of the compounds tested, the following resulted in at least 90% mortality at 10 ppm: 542.

TEST O

Test O followed an alternative protocol for evaluating control of Colorado potato beetle (*Leptinotarsa decemlineate*). Several hours prior to spraying, 5 mg (100% active ingredient, ai) of the test compounds were dissolved in 1 mL of acetone. Using the aqueous solution of 500 ppm of Ortho X-77™, the sample bottle was rinsed and added to the test compounds. This sample solution was then brought to 100 mL with the aqueous solution. Serial dilutions are made to obtain 50 mL of 10 ppm.

Formulated experimental compounds were sprayed to run-off on three week old potato or tomato plants. The plants were placed on a rotating turntable sprayer (10 rpm). Test solutions were applied using a flat fan air-assisted nozzle (Spraying Systems 122440) at 10 psi (69 KPa). Once the plants were dried, leaves were excised from the treated plant. The leaves were cut, and then the pieces were placed singly into a 5.5 cm-by-3.5 cm cell of a sixteen-well plastic tray. Each cell contained a 2.5 square of moistened chromatography paper to prevent desiccation. One second instar larvae was placed in each cell. At three days after infestation total number of dead Colorado potato beetles was recorded.

Of the compounds tested, the following resulted in at least 90% mortality at 10 ppm: 497, 500, 530, 543, 544, 558, 562 and 684.

TEST P

Seventy-eight cotton plants were grown in the greenhouse with natural lighting in Sassafras soil in six inch pots. When six true leaves were on the plant (approximately 36 cm tall) the soil was drenched with a solution of Compound 497, 500, 530, 531 or 543. Each of the 5 compounds was dissolved in 2 mL of acetone, and distilled water was added to make 300 ppm solutions of each of the compounds. The pots were divided into six groups (13 plants / treatment), and 10 mL of each solution was applied over the soil surface of each group with one group left untreated. The plants were arranged in the greenhouse in a randomized block design. Each treatment was divided into three groups for sampling at 24, 48, and 96 hours.

Leaves were taken from the base and terminal of the plants. The leaves from the third node and the terminal leaves greater than 15 cm^2 were sampled per plant. One clipped leaf from each plant was cut into four pieces and each piece was placed into an well with one second-instar larvae of *Heliothis virescens* (tobacco budworm). Larval mortality (%M) was recorded 96 hours after sampling. The percentage of leaf feeding (%FF) was also recorded. Consumption of the leaf in the well was reported as 0 – 100% (0 equals no feeding). Results are listed in Table P.

TABLE P

Percent Larval Mortality and Feeding of Cotton Leaves Over Time

Compound	Leaf position	24 h		48 h		96 h	
		% M	% FF	% M	% FF	% M	% FF
497	terminal	29	50	65	50	81	10
	base	13	80	46	100	59	20
500	terminal	4	60	38	60	30	30
	base	4	80	54	80	30	30
530	terminal	46	50	79	20	96	5
	base	33	80	63	50	70	5
531	terminal	25	40	42	40	55	10
	base	13	60	33	80	29	10
543	terminal	46	20	63	20	74	5
	base	33	30	58	30	17	5
Untreated	terminal	0	90	0	90	0	100
	base	0	90	0	100	0	95

TEST Q

For evaluating german cockroach (*Blatella germanica*), Compound 531 was mixed with water, and then blended into a slurry with equal amounts (by weight) of peanut butter. The mixture was air dried leaving a peanut butter bait with final concentration of the test

substance as indicated in the following table. Approximately 1 gram of bait was placed into each test cage. Ten German cockroaches (*Blatella germanica*) were then placed into each cage, and provided water via a saturated cotton ball. The cages were held indoors, with indirect sunlight, and temperatures ranging from 22 to 31 °C. Four test replicates were set up per rate. Evaluations were conducted 1, 2, 3, 5, and 7 days after treatment (DAT) by counting and removing the killed roaches found in each cage.

TABLE Q

German Cockroach Bait Test

Average of Killed Cockroaches					
Rate	1 DAT	2 DAT	3 DAT	5 DAT	7 DAT
untreated	0.3	0.3	0.3	1	2
400 ppm	3.8	5.8	6.3	7	7
2000 ppm	6.3	8	8.8	9	9
10000 ppm	9.5	9.5	9.5	9.5	9.5

TEST R

For evaluating control of fire ant (*Solenopsis xyloni*), Compound 531 was mixed with water and then mixed into a slurry with equal amounts (by weight) of Niban granular bait with no active ingredient (supplied by Nisus Corp.). The mixture was air dried, leaving a dry granular bait with final concentration of the test substance as indicated in the following table. The baits were uniformly sprinkled onto the sand substrate in each test cage. Fifty field-collected southern fire ants (*Solenopsis xyloni*) were then placed into each cage and provided water via a saturated cotton ball. The cages were held indoors with indirect sunlight and temperatures ranging from 22 to 31 °C. Four test replicates were set up per rate. Evaluations were conducted at 1, 3, 7, 10, and 14 days after treatment (DAT) by counting and removing the killed ants found in each cage.

TABLE R

Fire Ant Bait Test

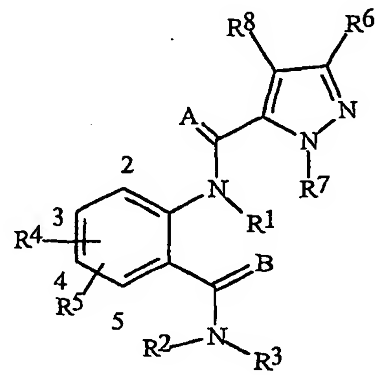
Average of Killed Fire Ants					
Rate	1 DAT	3 DAT	7 DAT	10 DAT	14 DAT
untreated	0.8	1.3	3.5	5.5	8.5
400 ppm	0.5	1.3	40.5	50	50
2,000 ppm	1	2	43	49.8	50
10,000 ppm	0	2.3	42.8	50	50

CLAIMS

What is claimed is:

1. A method for controlling for controlling lepidopteran, homopteran, hemipteran, thysanopteran and coleopteran insect pests, comprising:

contacting the insects or their environment with an arthropodicidally effective amount of a compound of Formula **I**, an *N*-oxide or an agriculturally suitable salt thereof



I

wherein

A and B are independently O or S;

R^1 is H, C_1–C_6 alkyl, C_2–C_6 alkoxycarbonyl or C_2–C_6 alkylcarbonyl;

R^2 is H or C_1–C_6 alkyl;

R^3 is H; C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, or C_3-C_6 cycloalkyl, each optionally substituted with one or more substituents selected from the group consisting of halogen, CN, NO_2, hydroxy, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_2-C_6 alkoxycarbonyl, C_2-C_6 alkylcarbonyl, C_3-C_6 trialkylsilyl, phenyl, phenoxy, 5-membered heteroaromatic rings, and 6-membered heteroaromatic rings; each phenyl, phenoxy, 5-membered heteroaromatic ring, and 6-membered heteroaromatic ring optionally substituted with one to three substituents independently selected from the group consisting of C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_3-C_6 cycloalkyl, C_1-C_4 haloalkyl, C_2-C_4 haloalkenyl, C_2-C_4 haloalkynyl, C_3-C_6 halocycloalkyl, halogen, CN, NO_2, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_4 alkylamino, C_2-C_8 dialkylamino, C_3-C_6 cycloalkylamino, C_4-C_8 (alkyl)(cycloalkyl)amino, C_2-C_4 alkylcarbonyl, C_2-C_6 alkoxycarbonyl, C_2-C_6 alkylaminocarbonyl, C_3-C_8 dialkylaminocarbonyl and C_3-C_6 trialkylsilyl; C_1-C_4

alkoxy; C_1-C_4 alkylamino; C_2-C_8 dialkylamino; C_3-C_6 cycloalkylamino; C_2-C_6 alkoxycarbonyl or C_2-C_6 alkylcarbonyl;

R^4 is H, C_1–C_6 alkyl, C_2–C_6 alkenyl, C_2–C_6 alkynyl, C_3–C_6 cycloalkyl, C_1–C_6 haloalkyl, CN, halogen, C_1–C_4 alkoxy, C_1–C_4 haloalkoxy or NO_2;

R^5 is H, C_1–C_6 alkyl, C_1–C_6 haloalkyl, C_1–C_4 alkoxyalkyl, C_1–C_4 hydroxyalkyl, $C(O)R^{10}$, CO_2R^{10}, $C(O)NR^{10}R^{11}$, halogen, C_1–C_4 alkoxy, C_1–C_4 haloalkoxy, $NR^{10}R^{11}$, $N(R^{11})C(O)R^{10}$, $N(R^{11})CO_2R^{10}$ or $S(O)_nR^{12}$;

R^6 is H, C_1–C_6 alkyl, C_1–C_6 haloalkyl, halogen, CN, C_1–C_4 alkoxy or C_1–C_4 haloalkoxy;

R^7 is C_1–C_6 alkyl, C_2–C_6 alkenyl, C_2–C_6 alkynyl, C_3–C_6 cycloalkyl, C_1–C_6 haloalkyl, C_2–C_6 haloalkenyl, C_2–C_6 haloalkynyl or C_3–C_6 halocycloalkyl; or

R^7 is a phenyl ring, a benzyl ring, a 5- or 6-membered heteroaromatic ring, a naphthyl ring system or an aromatic 8-, 9- or 10-membered fused heterobicyclic ring system, each ring or ring system optionally substituted with one to three substituents independently selected from R^9;

R^8 is H, C_1–C_6 alkyl, C_1–C_6 haloalkyl, halogen, C_1–C_4 alkoxy or C_1–C_4 haloalkoxy;

each R^9 is independently C_1–C_4 alkyl, C_2–C_4 alkenyl, C_2–C_4 alkynyl, C_3–C_6 cycloalkyl, C_1–C_4 haloalkyl, C_2–C_4 haloalkenyl, C_2–C_4 haloalkynyl, C_3–C_6 halocycloalkyl, halogen, CN, NO_2, C_1–C_4 alkoxy, C_1–C_4 haloalkoxy, C_1–C_4 alkylthio, C_1–C_4 alkylsulfinyl, C_1–C_4 alkylsulfonyl, C_1–C_4 alkylamino, C_2–C_8 dialkylamino, C_3–C_6 cycloalkylamino, C_4–C_8 (alkyl)(cycloalkyl)amino, C_2–C_4 alkylcarbonyl, C_2–C_6 alkoxycarbonyl, C_2–C_6 alkylaminocarbonyl, C_3–C_8 dialkylaminocarbonyl or C_3–C_6 trialkylsilyl;

R^{10} is H, C_1–C_4 alkyl or C_1–C_4 haloalkyl;

R^{11} is H or C_1–C_4 alkyl;

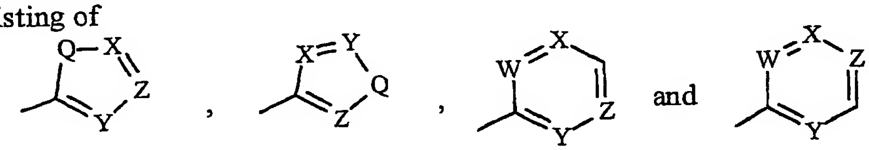
R^{12} is C_1–C_4 alkyl or C_1–C_4 haloalkyl; and

n is 0, 1 or 2.

2. The method of Claim 1 wherein

A and B are both O;

R^7 is a phenyl ring or a 5- or 6-membered heteroaromatic ring selected from the group consisting of



J-1 , J-2 , J-3 and J-4

each ring optionally substituted with one to three substituents independently selected from R^9;

Q is O, S, NH or NR^9; and

W, X, Y and Z are independently N, CH or CR^9, provided that in J-3 and J-4 at least one of W, X, Y or Z is N.

3. The method of Claim 2 wherein

R^1, R^2 and R^8 are all H;

R^3 is C_1–C_4 alkyl optionally substituted with halogen, CN, OCH_3 or $S(O)_pCH_3$;

R^4 group is attached at position 2;

R^4 is CH_3, CF_3, OCF_3, $OCHF_2$, CN or halogen;

R^5 is H, CH_3 or halogen;

R^6 is CH_3, CF_3 or halogen;

R^7 is phenyl or 2-pyridinyl, each optionally substituted; and

p is 0, 1 or 2.

4. The method of Claim 3 wherein

R^3 is C_1-C_4 alkyl and R^6 is CF_3.

5. The method of Claim 3 wherein

R^3 is C_1–C_4 alkyl and R^6 is Cl or Br.

6. The method of Claim 1 wherein the compound of Formula I is included in a composition further comprising an effective amount of at least one additional biologically active compound or agent.

7. The method of Claim 6 wherein the at least one additional biologically active compound or agent is selected from arthropodicides of the group consisting of pyrethroids, carbamates, neonicotinoids, neuronal sodium channel blockers, insecticidal macrocyclic lactones, γ–aminobutyric acid (GABA) antagonists, insecticidal ureas and juvenile hormone mimics.

8. The method of Claim 6 wherein the at least one additional biologically active compound or agent is selected from the group consisting of abamectin, acephate, acetamiprid, amidoflumet (S-1955), avermectin, azadirachtin, azinphos-methyl, bifenthrin, binfenazate, buprofezin, carbofuran, chlorfenapyr, chlorfluazuron, chlorpyrifos, chlorpyrifos-methyl, chromafenozide, clothianidin, cyfluthrin, beta-cyfluthrin, cyhalothrin, lambda-cyhalothrin, cypermethrin, cyromazine, deltamethrin, diafenthiuron, diazinon, diflubenzuron, dimethoate, diofenolan, emamectin, endosulfan, esfenvalerate, ethiprole, fenothicarb, fenoxycarb, fenpropathrin, fenproximate, fenvalerate, fipronil, flonicamid, flucythrinate, tau-fluvalinate, flufenerim (UR-50701), flufenoxuron, fonophos, halofenozide, hexaflumuron, imidacloprid, indoxacarb, isofenphos, lufenuron, malathion, metaldehyde, methamidophos, methidathion, methomyl, methoprene, methoxychlor, monocrotophos, methoxyfenozide, nithiazin, novaluron, noviflumuron (XDE-007), oxamyl, parathion, parathion-methyl, permethrin, phorate, phosalone, phosmet, phosphamidon, pirimicarb,

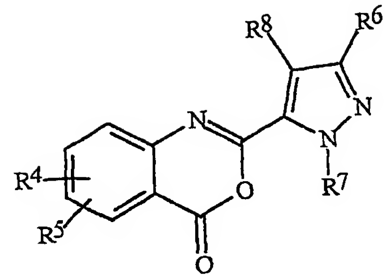
profenofos, pymetrozine, pyridalyl, pyriproxyfen, rotenone, spinosad, spiromesifin (BSN 2060), sulprofos, tebufenozide, teflubenzuron, tefluthrin, terbufos, tetrachlorvinphos, thiacloprid, thiamethoxam, thiodicarb, thiosultap-sodium, tralomethrin, trichlorfon and triflumuron, aldicarb, oxamyl, fenamiphos, amitraz, chinomethionat, chlorobenzilate, cyhexatin, dicofol, dienochlor, etoxazole, fenazaquin, fenbutatin oxide, fenpropathrin, fenpyroximate, hexythiazox, propargite, pyridaben, tebufenpyrad; and biological agents such as *Bacillus thuringiensis* including ssp. *aizawai* and *kurstaki*, *Bacillus thuringiensis* delta endotoxin, baculovirus, and entomopathogenic bacteria, virus and fungi.

9. The method of Claim 6 wherein the at least one additional biologically active compound or agent is selected from the group consisting of cypermethrin, cyhalothrin, cyfluthrin and beta-cyfluthrin, esfenvalerate, fenvalerate, tralomethrin, fenothicarb, methomyl, oxamyl, thiodicarb, clothianidin, imidacloprid, thiacloprid, indoxacarb, spinosad, abamectin, avermectin, emamectin, endosulfan, ethiprole, fipronil, flufenoxuron, triflumuron, diofenolan, pyriproxyfen, pymetrozine, amitraz, *Bacillus thuringiensis*, *Bacillus thuringiensis* delta endotoxin and entomophagous fungi.

10. The method of Claim 1 wherein at least one of the insect pests controlled is selected from the group consisting of *Alabama argillacea* Hübner (cotton leaf worm), *Archips argyrospila* Walker (fruit tree leaf roller), *A. rosana* Linnaeus (European leaf roller) and other *Archips* species, *Chilo suppressalis* Walker (rice stem borer), *Cnaphalocrosis medinalis* Guenee (rice leaf roller), *Crambus caliginosellus* Clemens (corn root webworm), *Crambus teterrellus* Zincken (bluegrass webworm), *Cydia pomonella* Linnaeus (codling moth), *Earias insulana* Boisduval (spiny bollworm), *Earias vittella* Fabricius (spotted bollworm), *Helicoverpa armigera* Hübner (American bollworm), *Helicoverpa zea* Boddie (corn earworm), *Heliothis virescens* Fabricius (tobacco budworm), *Herpetogramma licarsisalis* Walker (sod webworm), *Lobesia botrana* Denis & Schiffermüller (grape berry moth), *Pectinophora gossypiella* Saunders (pink bollworm), *Phyllocnistis citrella* Stainton (citrus leafminer), *Pieris brassicae* Linnaeus (large white butterfly), *Pieris rapae* Linnaeus (small white butterfly), *Plutella xylostella* Linnaeus (diamondback moth), *Spodoptera exigua* Hübner (beet armyworm), *Spodoptera litura* Fabricius (tobacco cutworm, cluster caterpillar), *Spodoptera frugiperda* J. E. Smith (fall armyworm), *Trichoplusia ni* Hübner (cabbage looper) and *Tuta absoluta* Meyrick (tomato leafminer), *Acyrthisiphon pisum* Harris (pea aphid), *Aphis craccivora* Koch (cowpea aphid), *Aphis fabae* Scopoli (black bean aphid), *Aphis gossypii* Glover (cotton aphid, melon aphid), *Aphis pomi* De Geer (apple aphid), *Aphis spiraecola* Patch (spirea aphid), *Aulacorthum solani* Kaltenbach (foxglove aphid), *Chaetosiphon fragaefolii* Cockerell (strawberry aphid), *Diuraphis noxia* Kurdjumov/Mordvilko (Russian wheat aphid), *Dysaphis plantaginea* Paaserini (rosy apple aphid), *Eriosoma lanigerum* Hausmann (woolly apple aphid), *Hyalopterus pruni* Geoffroy

(mealy plum aphid), *Lipaphis erysimi* Kaltenbach (turnip aphid), *Metopolophium dirrhodum* Walker (cereal aphid), *Macrosipum euphorbiae* Thomas (potato aphid), *Myzus persicae* Sulzer (peach-potato aphid, green peach aphid), *Nasonovia ribisnigri* Mosley (lettuce aphid), *Pemphigus* spp. (root aphids and gall aphids), *Rhopalosiphum maidis* Fitch (corn leaf aphid), *Rhopalosiphum padi* Linnaeus (bird cherry-oat aphid), *Schizaphis graminum* Rondani (greenbug), *Sitobion avenae* Fabricius (English grain aphid), *Therioaphis maculata* Buckton (spotted alfalfa aphid), *Toxoptera aurantii* Boyer de Fonscolombe (black citrus aphid), and *Toxoptera citricida* Kirkaldy (brown citrus aphid); *Adelges* spp. (adelgids); *Phylloxera devastatrix* Pergande (pecan phylloxera); *Bemisia tabaci* Gennadius (tobacco whitefly, sweetpotato whitefly), *Bemisia argentifolii* Bellows & Perring (silverleaf whitefly), *Dialeurodes citri* Ashmead (citrus whitefly) and *Trialeurodes vaporariorum* Westwood (greenhouse whitefly); *Empoasca fabae* Harris (potato leafhopper), *Laodelphax striatellus* Fallen (smaller brown planthopper), *Macrolestes quadrilineatus* Forbes (aster leafhopper), *Nephotettix cinticeps* Uhler (green leafhopper), *Nephotettix nigropictus* Stål (rice leafhopper), *Nilaparvata lugens* Stål (brown planthopper), *Peregrinus maidis* Ashmead (corn planthopper), *Sogatella furcifera* Horvath (white-backed planthopper), *Sogatodes orizicola* Muir (rice delphacid), *Typhlocyba pomaria* McAtee white apple leafhopper, *Erythroneoura* spp. (grape leafhoppers); *Magicidada septendecim* Linnaeus (periodical cicada); *Icerya purchasi* Maskell (cottony cushion scale), *Quadraspidiotus perniciosus* Comstock (San Jose scale); *Planococcus citri* Risso (citrus mealybug); *Pseudococcus* spp. (other mealybug complex); *Cacopsylla pyricola* Foerster (pear psylla), *Trioza diospyri* Ashmead (persimmon psylla), *Acrosternum hilare* Say (green stink bug), *Anasa tristis* De Geer (squash bug), *Blissus leucopterus leucopterus* Say (chinch bug), *Corythuca gossypii* Fabricius (cotton lace bug), *Cyrtopeltis modesta* Distant (tomato bug), *Dysdercus suturellus* Herrich-Schäffer (cotton stainer), *Euchistus servus* Say (brown stink bug), *Euchistus variolarius* Palisot de Beauvois (one-spotted stink bug), *Graptosthetus* spp. (complex of seed bugs), *Leptoglossus corculus* Say (leaf-footed pine seed bug), *Lygus lineolaris* Palisot de Beauvois (tarnished plant bug), *Nezara viridula* Linnaeus (southern green stink bug), *Oebalus pugnax* Fabricius (rice stink bug), *Oncopeltus fasciatus* Dallas (large milkweed bug), *Pseudatomoscelis seriatus* Reuter (cotton fleahopper), *Frankliniella occidentalis* Pergande (western flower thrip), *Scirthothrips citri* Moulton (citrus thrip), *Sericothrips variabilis* Beach (soybean thrip), and *Thrips tabaci* Lindeman (onion thrip), *Leptinotarsa decemlineata* Say (Colorado potato beetle), *Epilachna varivestis* Mulsant (Mexican bean beetle) and wireworms of the genera *Agriotes*, *Athous* or *Limonius*).

11. A benzoxazinone compound of Formula **10**



10

wherein

R^4 is H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_1-C_6 haloalkyl, CN, halogen, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy or NO_2;

R^5 is H, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_4 alkoxyalkyl, C_1-C_4 hydroxyalkyl, $C(O)R^{10}$, CO_2R^{10}, $C(O)NR^{10}R^{11}$, halogen, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, $NR^{10}R^{11}$, $N(R^{11})C(O)R^{10}$, $N(R^{11})CO_2R^{10}$ or $S(O)_nR^{12}$;

R^6 is H, C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, CN, C_1-C_4 alkoxy or C_1-C_4 haloalkoxy;

R^7 is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_1-C_6 haloalkyl, C_2-C_6 haloalkenyl, C_2-C_6 haloalkynyl or C_3-C_6 halocycloalkyl; or

R^7 is a phenyl ring, a benzyl ring, a 5- or 6-membered heteroaromatic ring, a naphthyl ring system or an aromatic 8-, 9- or 10-membered fused heterobicyclic ring system, each ring or ring system optionally substituted with one to three substituents independently selected from R^9;

R^8 is H, C_1–C_6 alkyl, C_1–C_6 haloalkyl, halogen, C_1–C_4 alkoxy or C_1–C_4 haloalkoxy;

each R^9 is independently C_1–C_4 alkyl, C_2–C_4 alkenyl, C_2–C_4 alkynyl, C_3–C_6 cycloalkyl, C_1–C_4 haloalkyl, C_2–C_4 haloalkenyl, C_2–C_4 haloalkynyl, C_3–C_6 halocycloalkyl, halogen, CN, NO_2, C_1–C_4 alkoxy, C_1–C_4 haloalkoxy, C_1–C_4 alkylthio, C_1–C_4 alkylsulfinyl, C_1–C_4 alkylsulfonyl, C_1–C_4 alkylamino, C_2–C_8 dialkylamino, C_3–C_6 cycloalkylamino, C_4–C_8 (alkyl)(cycloalkyl)amino, C_2–C_4 alkylcarbonyl, C_2–C_6 alkoxycarbonyl, C_2–C_6 alkylaminocarbonyl, C_3–C_8 dialkylaminocarbonyl or C_3–C_6 trialkylsilyl;

R^{10} is H, C_1–C_4 alkyl or C_1–C_4 haloalkyl;

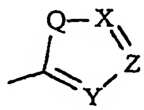
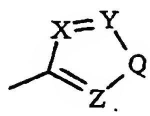
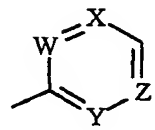
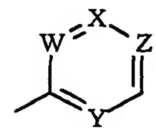
R^{11} is H or C_1–C_4 alkyl;

R^{12} is C_1–C_4 alkyl or C_1–C_4 haloalkyl; and

n is 0, 1 or 2.

12. The compound of Claim 11 wherein

R^7 is a phenyl ring or a 5- or 6-membered heteroaromatic ring selected from the group consisting of

 ,  ,  and  ,

J-1 J-2 J-3 J-4

each ring optionally substituted with one to three substituents independently selected from R^9;

Q is O, S, NH or NR^9; and

W, X, Y and Z are independently N, CH or CR^9, provided that in J-3 and J-4 at least one of W, X, Y or Z is N.

13. The compound of Claim 12 wherein

R^8 is H;

R^4 group is attached at position 2;

R^4 is CH_3, CF_3, OCF_3, $OCHF_2$, CN or halogen;

R^5 is H, CH_3 or halogen;

R^6 is CH_3, CF_3 or halogen; and

R^7 is phenyl or 2-pyridinyl, each optionally substituted.

14. The compound of Claim 13 wherein R^6 is CF_3.

15. The compound of Claim 13 wherein R^6 is Cl or Br.

16. The compounds of Claim 11 wherein

R^4 is at the 2 position and is CH_3, Cl or Br;

R^5 is at the 4 position and is F, Cl, Br, I or CF_3;

R^6 is CF_3, Cl or Br;

R^7 is 3-Cl-2-pyridinyl or 3-Br-2-pyridinyl; and

R^8 is H.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 02/25613

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A01N43/56 C07D401/04 C07D231/16 C07D231/14 C07D413/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	NL 9 202 078 A (RIJKSLANDBOUWHOGESCHOOL) 16 June 1994 (1994-06-16) cited in the application the whole document	1-10
X	JP 2001 019691 A (NISSAN CHEM IND LTD) 23 January 2001 (2001-01-23) examples	11-13,15
P,X	WO 01 70671 A (DU PONT ;LAHM GEORGE P (US); MYERS BRIAN J (US); SELBY THOMAS P (U) 27 September 2001 (2001-09-27) table 9	1-10

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
7 November 2002	15/11/2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	De Jong, B

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 02/25613

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 02 48115 A (MYERS BRIAN JAMES ;SELBY THOMAS PAUL (US); STEVENSON THOMAS MARTIN) 20 June 2002 (2002-06-20) scheme 7 example 2 -----	11-16

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 02/25613

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			WO	0170671 A2	27-09-2001
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			WO	0248115 A2	20-06-2002